

Spivack 10\_080043 - - Inventor Search History

=> d his ful l18-

FILE 'HCAPLUS' ENTERED AT 12:09:13 ON 25 AUG 2006

L20 19 SEA ABB=ON PLU=ON YOA PU HU O/AU OR YOA PU HU OLIVER/AU OR  
HU O Y P/AU OR HU O YOA PU/AU OR HU OLIVER O Y/AU OR HU OLIVER  
Y P?/AU  
D STAT QUE L20  
D IBIB ABS L20 1-19

L21 13 SEA ABB=ON PLU=ON (HSIONG C H/AU OR HSIONG CHENG HUEI/AU)  
NOT L20  
D STAT QUE L21  
D IBIB ABS L21 1-13

L22 17 SEA ABB=ON PLU=ON (KUO B/AU OR ("KUO BENJAMIN P"/AU OR "KUO  
BENJAMIN PEI CHUNG"/AU)) NOT L20 OR L21  
D STAT QUE L22  
D IBIB ABS HITSTR L22 1-17

L23 17 SEA ABB=ON PLU=ON (PAO L/AU OR PAO L H/AU OR PAO LI HENG/AU  
OR PAO H/AU) NOT (L20 OR L21 OR L22)  
D STAT QUE L23  
D IBIB ABS L23 1-17

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 24 AUG 2006 HIGHEST RN 904307-87-5

DICTIONARY FILE UPDATES: 24 AUG 2006 HIGHEST RN 904307-87-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCAPLUS

Copyright of the articles to which records in this database refer is  
held by the publishers listed in the PUBLISHER (PB) field (available  
for records published or updated in Chemical Abstracts after December  
26, 1996), unless otherwise indicated in the original publications.  
The CA Lexicon is the copyrighted intellectual property of the  
the American Chemical Society and is provided to assist you in searching  
databases on STN. Any dissemination, distribution, copying, or storing  
of this information, without the prior written consent of CAS, is  
strictly prohibited.

FILE COVERS 1907 - 25 Aug 2006 VOL 145 ISS 10

FILE LAST UPDATED: 24 Aug 2006 (20060824/ED)

Spivack 10\_080043 - - Inventor Search History

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=>

=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 12:09:13 ON 25 AUG 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 25 Aug 2006 VOL 145 ISS 10

FILE LAST UPDATED: 24 Aug 2006 (20060824/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

=>

=> d stat que 120

L20 19 SEA FILE=HCAPLUS ABB=ON PLU=ON YOA PU HU O/AU OR YOA PU HU  
OLIVER/AU OR HU O Y P/AU OR HU O YOA PU/AU OR HU OLIVER O Y/AU  
OR HU OLIVER Y P?/AU

=>

=>

=> d ibib abs 120 1-19

L20 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:361861 HCAPLUS

DOCUMENT NUMBER: 142:540

TITLE: Antinociceptive effect of a novel long-acting  
nalbuphine preparation

AUTHOR(S): Liu, K. S.; Hu, O. Y. P.; Ho, S. T.; Tzeng,  
J. I.; Chen, Y. W.; Wang, J. J.

CORPORATE SOURCE: Department of Medical Research, Department of  
Chemistry, Chi-Mei Medical Center, National Cheng Kung  
University, Tainan, Taiwan

SOURCE: British Journal of Anaesthesia (2004), 92(5), 712-715  
CODEN: BJANAD; ISSN: 0007-0912

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Background: A long-acting analgesic may be particularly desirable in patients suffering from long-lasting pain. The aim of the study was to evaluate the antinociceptive effect of a novel nalbuphine preparation and to determine its duration of action. Methods: The antinociceptive effects of i.m. nalbuphine HCl in saline and nalbuphine base in sesame oil were evaluated in rats. The in vitro drug-releasing profiles of nalbuphine HCl and base

Spivack 10\_080043-- Inventor Search--

in different preps. were also evaluated. Results: We found that i.m. nalbuphine HCl 25, 50 and 100  $\mu\text{mol kg}^{-1}$  produced dose-related antinociceptive effects with a duration of action of 1.5, 2 and 3 h, resp. I.M. nalbuphine base 100, 200 and 400  $\mu\text{mol kg}^{-1}$  also produced dose-related antinociceptive effects but with longer durations of action: 27, 49 and 55 h, resp. In vitro studies demonstrated that nalbuphine base in sesame oil had the slowest drug-releasing profile of the different preps. Conclusions: I.M. injection of an oil formulation of nalbuphine base produced a long-lasting antinociceptive effect.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:859553 HCAPLUS

DOCUMENT NUMBER: 140:228370

TITLE: Pharmacokinetics of sevoflurane uptake into the brain and body

AUTHOR(S): Lu, C. C.; Tsai, C. S.; Ho, S. T.; Chen, W. Y.; Wong, C. S.; Wang, J. J.; Hu, O. Y. P.; Lin, C. Y.

CORPORATE SOURCE: Department of Anaesthesiology, Tri-Service General Hospital/ National Defense Medical Center, Taipei, Taiwan

SOURCE: Anaesthesia (2003), 58(10), 951-956

CODEN: ANASAB; ISSN: 0003-2409

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this study was to investigate the pharmacokinetics of sevoflurane uptake into the brain and body by comparing sevoflurane concns. in internal jugular-bulb blood (Jsev), arterial blood (Asev) and pulmonary arterial blood (PAsev) over a fixed inspired sevoflurane concentration

Ten patients (aged 51-73 yr), undergoing coronary artery bypass grafting surgery, were enrolled in this study. They were anesthetized using a constant 3.5% inspired sevoflurane concentration (CIsev) during the first hour of

anesthesia. During constant volume-controlled ventilation, we measured CIsev and end-tidal sevoflurane (CEsev) using IR anal. The sevoflurane concentration in the blood was analyzed using gas chromatog., and cardiac output was measured using an Opti-Q pulmonary artery catheter. We found that it took 40 min for the brain concentration to equilibrate with arterial blood (Asev). Both CIsev-CEsev and Asev-PAsev gradients persisted during the study period. There was no further uptake of sevoflurane into the brain after 40 min; however, there was near-constant uptake into the body.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:696526 HCAPLUS

DOCUMENT NUMBER: 139:207740

TITLE: Dermal cytochrome P450 1A inhibitors and enhancers

INVENTOR(S): Yoa-Pu, Hu Oliver; Hsiong, Cheng-Huei; Wang, Chao-Jih; Pao, Li-Heng

PATENT ASSIGNEE(S): Taiwan

SOURCE: U.S. Pat. Appl. Publ., 12 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003166583	A1	20030904	US 2002-79416	20020222
PRIORITY APPLN. INFO.:			US 2002-79416	20020222

AB The present invention provides dermal cytochrome P 450 1A (CYP1A) inhibitors, which include free base or pharmacol. acceptable salt of (-)- and (+)-epicatechin, (+)-limonene, 3-phenylpropyl acetate,  $\alpha$ - and  $\beta$ -naphthoflavone, apigenin, baicalein, baicalin,  $\beta$ -myrcene, catechin, etc. The CYP1A inhibitors can be co-administered with compds. with first-pass effect such as dermatol. drugs to improve the bioavailability of the drugs. The present invention also provides dermal CYP 1 A enhancers, which include (+)-catechin, (-)- and (+)-epicatechin, (+)-limonene, 3-phenylpropyl acetate, apigenin, baicalein, baicalin, etc. Examples were given showing the inhibitory effects on liver CHPla activity of the compds.

L20 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:303496 HCAPLUS

DOCUMENT NUMBER: 139:399518

TITLE: Biodegradable polymeric microspheres for nalbuphine prodrug controlled delivery: in vitro characterization and in vivo pharmacokinetic studies

AUTHOR(S): Liu, Fang-I.; Kuo, J. H.; Sung, K. C.; Hu, Oliver Y. P.

CORPORATE SOURCE: Department of Pharmacy, Chia-Nan University of Pharmacy and Science, Tainan Hsien, 717, Taiwan

SOURCE: International Journal of Pharmaceutics (2003), 257(1-2), 23-31

CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The objective of this work was to study the in vitro characteristics as well as in vivo pharmacokinetic performance of a series nalbuphine (NA) prodrug-loaded microspheres. An oil-in-water solvent evaporation method was used to incorporate the various NA prodrugs into poly(d,l-lactide-co-glycolide) (PLGA)-based microspheres. The morphol. of microspheres under the SEM revealed a spherical shape with smooth surface. Drug release rates for the microspheres were found to be a function of prodrug hydrophilicity, with higher drug release rates for microspheres loaded with more hydrophilic prodrugs. The release profiles fit well to the Baker and Lonsdale's spherical matrix model, suggesting the drug release from microspheres was consistent with a diffusion mechanism. The in vivo pharmacokinetic studies after s.c. injection of microspheres into rabbits showed sustained plasma NA-time profiles, with approx. 104.7, 67.2, and 41.0% relative bioavailability for microspheres loaded with nalbuphine propionate (NAP), nalbuphine pivalate (NPI), and nalbuphine decanoate (NDE), resp. The in vitro release characteristics correlated well with the in vivo pharmacokinetic profiles. The results indicated that the prodrug hydrophilicity had significant effects on the in vitro as well as in vivo drug release kinetics. The present study demonstrates the feasibility of using biodegradable polymeric microspheres for controlled delivery of NA prodrugs.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:672107 HCAPLUS

DOCUMENT NUMBER: 134:227211

TITLE: Regional absorption of nalbuphine and its prodrug in rats  
 AUTHOR(S): Pao, L. -H.; Chou, R. -M.; Hu, Oliver O. -Y.  
 CORPORATE SOURCE: School of Pharmacy, National Defense Medical Center, NeiHu, Taiwan  
 SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (2000), 27th, 415-416  
 CODEN: PCRMEY; ISSN: 1022-0178  
 PUBLISHER: Controlled Release Society, Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Nalbuphine is an effective analgesic for relief of moderate to severe pain, and the side effects of nalbuphine, such as addiction and respiratory depression, are much less than those of morphine and narcotics. Prodrug design appears to be a feasible approach to deliver nalbuphine orally. A study was conducted to investigate and compare regional absorption of nalbuphine and its three prodrugs in three segments of the rat intestine using in situ closed-loop model to access the potential of the development of oral controlled-release dosage form of nalbuphine and its prodrugs. Results showed that nalbuphine HCl is well absorbed along the small intestine as well as in the colon, which is a potential candidate for development of oral controlled release dosage form. Poor solubility of nalbuphine prodrugs might limit its absorption from the gastrointestinal tract.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:637540 HCAPLUS  
 DOCUMENT NUMBER: 134:25080  
 TITLE: High-performance liquid chromatographic method for the simultaneous determination of nalbuphine and its prodrug, sebacoyl dinalbuphine ester, in dog plasma and application to pharmacokinetic studies in dogs  
 AUTHOR(S): Pao, L.-H.; Hsiong, C.-H.; Hu, O. Y.-P.; Ho, S.-T.  
 CORPORATE SOURCE: School of Pharmacy, National Defense Medical Center, Taipei, Taiwan  
 SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (2000), 746(2), 241-247  
 CODEN: JCBEBP; ISSN: 0378-4347  
 PUBLISHER: Elsevier Science B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB For the determination of nalbuphine and its long acting prodrug, sebacoyl dinalbuphine ester (SDN), in biol. samples, a reversed-phase high-performance liquid chromatog. method using dual detectors was established. UV and fluorescence detectors were connected in series for determining SDN and nalbuphine, resp. The two analytes and internal standard were extracted from plasma by alkaline liquid-liquid extraction using n-hexane-isoamyl alc. (9:1, volume/volume). The calibration curve for nalbuphine was linear over the range from 10 to 2500 ng/mL, while the range was 25 to 2500 ng/mL for SDN. The within- and between-day precision and accuracy were all within 10% for both nalbuphine and SDN over these concns. The method was applied successfully to a pharmacokinetic study of SDN administered at 20 mg/kg to two beagle dogs. Pharmacokinetic anal. revealed that SDN followed a linear one-compartment model with an elimination half-life of 74.7 min.

Formation of nalbuphine after i.v. administration of SDN was observed in the first time point sample (5 min). These results indicate that SDN is rapidly metabolized to its active moiety, nalbuphine, in dogs and no other metabolites are detected in plasma.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:249437 HCAPLUS

DOCUMENT NUMBER: 133:155296

TITLE: Delivery of nalbuphine and its prodrugs across skin by passive diffusion and iontophoresis

AUTHOR(S): Sung, K. C.; Fang, J.-Y.; Yoa-Pu Hu, O.

CORPORATE SOURCE: Department of Pharmacy, Chia Nan College of Pharmacy and Science, Tainan Hsien, Taiwan

SOURCE: Journal of Controlled Release (2000), 67(1), 1-8  
CODEN: JCREEC; ISSN: 0168-3659

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The in vitro transport of nalbuphine (NA) and its prodrugs across various skins was investigated in order to assess the effects of prodrug lipophilicity on passive as well as iontophoretic permeation. The passive diffusion of NA and its prodrugs increased with the drug lipophilicity. Iontophoresis significantly increased the transport of NA and its prodrugs; the enhancement ratio was highest for NA and decreased as the drug lipophilicity increased. Measurements using intact and stratum corneum (SC)-stripped skins showed that the SC was the major skin diffusion barrier for the passive permeation of NA and nalbuphine pivalate (NAP). The iontophoretic permeation of NA and NAP across intact and SC-stripped skins indicated that the SC layer was not rate-limiting for the permeation of NA, but remained the rate-limiting barrier for transdermal permeation of NAP. Permeation studies using SC-stripped skins suggested that the intercellular pathway was the predominant route for the passive permeation of NA and NAP as well as the iontophoretic permeation of NAP across the SC. The relative rates of passive and iontophoretic permeation across Wistar rat skins demonstrated that a significant amount of NA may permeate skin via the appendageal routes, whereas NAP permeated predominantly through the lipid matrix.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:191639 HCAPLUS

DOCUMENT NUMBER: 133:68211

TITLE: Does Chinese ethnicity affect the pharmacokinetics and pharmacodynamics of angiotensin-converting enzyme inhibitors?

AUTHOR(S): Ding, P. Y. A.; Hu, O. Yoa-Pu; Pool, P. E.;  
Liao, W.-C.

CORPORATE SOURCE: Department of Internal Medicine, Veterans General Hospital-Taipei, Taipei, Taiwan

SOURCE: Journal of Human Hypertension (2000), 14(3), 163-170  
CODEN: JHHYEN; ISSN: 0950-9240

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 53 refs. Information from clin. and pharmacokinetic studies of angiotensin-converting enzyme inhibitors (ACEIs) has come from subjects who are mostly male and Caucasian, but the use of ACEIs extends to

populations worldwide. Significant differences between Chinese in general and male Caucasians have been demonstrated in the pharmacokinetics/dynamics of other drug classes, and this could have implications for the use of ACEIs in the Chinese population. These include: significant Chinese/Caucasian genetic variation in the renin-angiotensin system based on an insertion/deletion polymorphism of the ACE gene; the genetic regulation of plasma ACE activity in the Chinese population; and genetic factors involving hypertension which may also influence the response to treatment. Oral and i.v. pharmacokinetic data from various studies of Chinese and Caucasian subjects are available for cilazapril, fosinopril, and perindopril, and pharmacodynamic data are available for eight different ACEIs. Based on these data, there are few differences in the pharmacokinetics of ACEIs between Chinese and Caucasians. Most ACEIs showed good blood-pressure-lowering efficacy in Chinese (benazepril, enalapril, fosinopril and spirapril), with perhaps less efficacy of cilazapril or a relatively shorter-term effect with cilazapril or perindopril, compared to Caucasians. Chinese experience more cough from ACEIs (captopril and enalapril) than Caucasians. Data suggest that fosinopril may not induce cough in as many subjects as do other ACEIs, and this seems to be true of Chinese as well. The mechanism, currently unknown, could involve fosinopril's dual elimination pathway (hepatic and renal). Pharmacokinetic data also support the use of fosinopril in congestive heart failure where elimination pathways may be impaired. In conclusion, ethnic differences between Chinese and Caucasians with respect to ACE and angiotensin gene polymorphism, which might be expected to differentially affect the action of ACEIs in these two ethnic groups, do not, in fact, have such an effect. Rather, differences among the ACEIs appear to be more important.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:28398 HCAPLUS

DOCUMENT NUMBER: 130:316549

TITLE: Mucoadhesive buccal disks for novel nalbuphine prodrug controlled delivery: effect of formulation variables on drug release and mucoadhesive performance

AUTHOR(S): Han, Rough-Yee; Fang, Jia-You; Sung, K. C.; Hu, Oliver Y. P.

CORPORATE SOURCE: Department of Pharmacy, Chia-Nan College of Pharmacy and Science, Tainan Hsien, Taiwan

SOURCE: International Journal of Pharmaceutics (1999), 177(2), 201-209

CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of drug solubility and loading percent, as well as Carbopol 934/hydroxypropyl cellulose (CP/HPC) ratio, on drug release and mucoadhesive performance of the nalbuphine prodrug loaded buccal disks were assessed. Drug release rates for the disks were found to be a function of drug solubility, with higher drug release rates for disks loaded with more hydrophilic prodrugs and an increased amount of  $\beta$ -cyclodextrin. The drug release rates increased with loading percents for nalbuphine hydrochloride, whereas an opposite drug release trend was observed for disks loaded with nalbuphine enanthate, which can be explained by the diffusional drug release mechanism. The CP/HPC ratio affected release rates of nalbuphine enanthate, whereas the ratio had no impact on the release of nalbuphine hydrochloride. Within the 2 days of experiment time, all formulations attached well to the porcine buccal tissues,



indicating those formulation variables had no influence on the mucoadhesive performance of CP/HPC-based buccal disks.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:563984 HCAPLUS

DOCUMENT NUMBER: 130:43189

TITLE: Controlled release of nalbuphine prodrugs from biodegradable polymeric matrixes: influence of prodrug hydrophilicity and polymer composition

AUTHOR(S): Sung, K. C.; Han, Rough-Yee; Hu, Oliver Y. P.; Hsu, Li-Ren

CORPORATE SOURCE: Department of Pharmacy, Chia-Nan College of Pharmacy and Science, Tainan Hsien, Taiwan

SOURCE: International Journal of Pharmaceutics (1998), 172(1-2), 17-25

CODEN: IJPHDE; ISSN: 0378-5173

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The objective of this work was to assess the effects of nalbuphine prodrug hydrophilicity and lactide/glycolide copolymer ratio on drug release from lactide/glycolide based polymeric matrixes. A panel of 4 nalbuphine prodrugs with various ester chains were incorporated into polylactide-based matrixes by using the solvent evaporation method. Drug release rates for the matrixes were a function of prodrug hydrophilicity, with higher drug release rates for matrixes with more hydrophilic prodrugs. Data anal. using the Higuchi expression indicated that the release of various prodrugs from polylactide based matrixes was consistent with a diffusion mechanism. The prodrug release rate consts. derived from the Higuchi expression correlated well with prodrug solubilities. In the second part of the study, the effect of lactide/glycolide copolymer ratio on nalbuphine propionate release was studied. The drug release rate and matrix hydration rate were a function of copolymer ratio, with faster drug release and matrix hydration for matrixes with lower lactide/glycolide ratio copolymers. The nalbuphine propionate release profiles fit well to the Higuchi expression, indicating that drug release from the poly(lactide-co-glycolide)-based matrixes was consistent with a diffusion mechanism. The drug release rates correlated well with matrix hydration rates, suggesting that different polymer compns. may attribute to various matrix hydration and therefore affect drug release from the poly(lactide-co-glycolide) matrixes.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:448454 HCAPLUS

DOCUMENT NUMBER: 129:197692

TITLE: Phase II and pharmacokinetic study of paclitaxel therapy for unresectable hepatocellular carcinoma patients

AUTHOR(S): Chao, Y.; Chan, W. -K.; Birkhofer, M. J.; Hu, O. Y. -P.; Wang, S. -S.; Huang, Y. -S.; Liu, M.; Whang-Peng, J.; Chi, K. -H.; Lui, W. -Y.; Lee, S. -D.

CORPORATE SOURCE: Division of Gastroenterology, Veterans General Hospital-Taipei and School of Medicine, National Yang-Ming University, Taipei, 11217, Taiwan

SOURCE: British Journal of Cancer (1998), 78(1), 34-39  
CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Churchill Livingstone  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB This phase II clin. study investigated the efficacy, toxicity and pharmacokinetics of paclitaxel in hepatocellular carcinoma (HCC) patients. Twenty patients with measurable, unresectable HCC, normal serum bilirubin, and normal bone marrow and renal functions were studied. Paclitaxel was given i.v. at 175 mg/m<sup>2</sup> over 3 h every 3 wk. No complete or partial responses were observed. Five patients had stable disease. Major treatment toxicities (grade 3-4) were neutropenia (25%), thrombocytopenia (15%), infection (10%) and allergy (10%). Treatment-related deaths occurred in 2 patients. The median survival was 12 wk (range 1-36). Paclitaxel is metabolized by the liver, and the pharmacokinetics of paclitaxel in cancer patients with liver involvement or impairment may be important clin. The paclitaxel area under the concentration-time curve was increased, clearance was lower, and treatment-related deaths were higher in patients with hepatic impairment. In conclusion, paclitaxel in this dose and schedule has no significant anticancer effect in HCC patients. Paclitaxel should be used with caution in cancer patients with liver impairment.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:300592 HCAPLUS

DOCUMENT NUMBER: 129:8605

TITLE: Nalbuphine esters having long-acting analgesic action and method of use

INVENTOR(S): Yoa-Pu, Hu Oliver; Wang, Jhi-Joung; Ho, Shung-Tai

PATENT ASSIGNEE(S): National Science Council, Taiwan

SOURCE: U.S., 42 pp., Cont.-in-part of U.S. Ser. No. 161,257, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5750534	A	19980512	US 1996-690361	19960726
PRIORITY APPLN. INFO.:			US 1994-161257	B2 19940316

OTHER SOURCE(S): MARPAT 129:8605

AB Long-acting analgesic nalbuphine prodrugs and pharmaceutical compns. comprising the nalbuphine prodrugs are described. These prodrugs are long-acting analgesics when administered i.m., s.c., orally, or transdermally. Five esters of nalbuphine were prepared and pharmacodynamic studies were performed with rats. For example, nalbuphine decanoate was i.m. injected on the ears of rabbits at 0.25 mg/kg; the analgesic duration of nalbuphine decanoate was increased 30 times over the nalbuphine hydrochloride.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:601460 HCAPLUS

DOCUMENT NUMBER: 123:202

TITLE: Plasma and red blood cell pharmacokinetics of pimobendan enantiomers in healthy Chinese

AUTHOR(S): Chu, K. -M.; Shieh, S. -M.; Hu, O. Y. -P.

CORPORATE SOURCE: National Defense Medical Center, Institute Medical Sciences, Taipei, Taiwan

SOURCE: European Journal of Clinical Pharmacology (1995), 47(6), 537-42

CODEN: EJCPAS; ISSN: 0031-6970

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetics of enantiomers of pimobendan and their demethylated metabolites in plasma and red cells were studied in 8 normal healthy volunteers. After racemic pimobendan 5 mg IV, the plasma concentration-time curve followed a two-compartment open-model with elimination half-lives of 1.81 h and 1.86 h for (+)- and (-)-pimobendan, resp. The clearances and vols. of distribution postequil. were 13.5 mL $\Sigma$ min<sup>-1</sup> $\Sigma$ kg<sup>-1</sup>, 14.4 mL $\Sigma$ min<sup>-1</sup> $\Sigma$ kg<sup>-1</sup>; 1.741 $\Sigma$ kg<sup>-1</sup> and 2.34 l $\Sigma$ kg<sup>-1</sup> for (+)- and (-)-pimobendan, resp. Plasma protein binding (n = 3) of (+)-, (-)-pimobendan, (+)- and (-)-demethylated metabolites was 97.6, 97.6, 92.2 and 92.5%, resp. The plasma concentration-time curve also followed a two-compartment open model after oral administration of 7.5 mg racemic pimobendan. The absolute bioavailabilities of (+)- and (-)-pimobendan were 0.51 and 0.55. Peak levels of (+)- and (-)-pimobendan, both at 1.2 h, were 15.8 and 16.8 ng $\Sigma$ mL<sup>-1</sup>, resp. The (+)- and (-)-pimobendan concns. in red cells were determined and their pharmacokinetics were estimated using

red

blood cell data. Interesting phenomena were observed: the peak concns. of (+)- and (-)-pimobendan in red blood cells were about 5.5- and 9.2-times higher than in plasma, and the AUCs were correspondingly elevated. The volume of distribution of the central compartment of (-)-pimobendan in red cell was significantly smaller than that of (+)-pimobendan. (0.24 Vs. 0.42 l $\Sigma$ kg<sup>-1</sup>). Similar phenomena were found after IV administration. These all indicated stereoselective partitioning or distribution of (-)-pimobendan into red cells. Since the elimination half-life of (+)- and (-)-pimobendan in red cells was similar (3.07 vs. 2.97 h), the highly significant difference in clearance between (+)- and (-)-pimobendan (3.7 vs. 2.3 mL $\Sigma$ min<sup>-1</sup> $\Sigma$ kg<sup>-1</sup>) was solely due to the stereoselective distribution of (-)-pimobendan into the red blood cells. This stereoselective property of the (-)-isomer may be the explanation of a previous report that (-)-pimobendan produced a 1.5-times larger contractile force in detergent-skinned preps. of cardiac muscle from guinea pig and dog than the (+)-isomer.

L20 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:521071 HCAPLUS

DOCUMENT NUMBER: 122:281284

TITLE: Determination of anticancer drug vitamin K3 in plasma by high-performance liquid chromatography

AUTHOR(S): Hu, Oliver Y.-P.; Wu, Chih-Yuan; Chan, Win-Kai; Wu, Felicia Y.-H.

CORPORATE SOURCE: School of Pharmacy, National Defense Medical Center, Taipei, 100, Taiwan

SOURCE: Journal of Chromatography, B: Biomedical Applications (1995), 666(2), 299-305

CODEN: JCBEP; ISSN: 0378-4347

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Synthetic vitamin K3 (VK3, 2-methyl-1,4-naphthoquinone, or menadione) has been found to exhibit antitumor activity against various human cancer cells at relative high dose. Parallel to our study on the mechanism of VK3 action and for future clin. trials in Taiwan, we developed a simple, sensitive and accurate high-performance liquid chromatog. method for the

determination of VK3 in biol. fluids. VK3 was extracted from the plasma samples with

n-hexane. The chromatog. separation employed an ODS anal. column (5  $\mu$ m, 250+4.6 mm I.D.) with a mobile phase of methanol-water (70:30, volume/volume) and UV detection at 265 nm. On completely drying of the extraction

solution, n-hexane, by a stream of nitrogen, menadione was lost to a great extent. Methanol (70%, 200  $\mu$ l) was added to the extraction solvent after extraction and centrifugation to prevent the loss of menadione. The absolute recovery was  $82.4 \pm 7.69\%$  ( $n = 7$ ). The within-day and between-day calibration curves of VK3 in plasma in the ranges of interest (0.01-10.00  $\mu$ g/mL; 0.01-5.00  $\mu$ g/mL) showed good linearity ( $r > 0.999$ ) and acceptable precision. The limit of quantitation of VK3 was 10 ng/mL in plasma. This method has been successfully applied to a pilot pharmacokinetic study of VK3 in rabbits receiving an i.v. high-dose bolus injection of 75 mg menadiol sodium diphosphate (Synkayvite). The pharmacokinetic properties of menadione could be described adequately by an open two-compartment model. The mean half-life of menadiol (transformation to menadione) was  $2.60 \pm 0.12$  min. The elimination half-life, volume of distribution and plasma clearance of menadione were  $26.3 \pm 2.97$  min,  $25.7 \pm 0.78$  l, and  $0.68 \pm 0.10$  l/min, resp.

L20 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:525968 HCAPLUS

DOCUMENT NUMBER: 113:125968

TITLE: A third, "deep," compartment for phenothiazine drug disposition: a new look at an old problem

AUTHOR(S): Curry, Stephen H.; Hu, Oliver Y. P.

CORPORATE SOURCE: J. Hills Miller Health Cent., Univ. Florida, Gainesville, FL, 32610, USA

SOURCE: Psychopharmacology Bulletin (1990), 26(1), 95-8  
CODEN: PSYBB9; ISSN: 0048-5764

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Volunteers were given oral promazine doses, and blood and urine were collected for promazine assay for as long as was necessary for the drug to cease to be detectable. Postabsorption data were subjected to two- and three-compartment modeling. Renal clearance was calculated. Renal excretion data were analyzed by use of the sigma-minus method, which permits the calcn. of the half-life in plasma from excretion data. The mean  $\alpha$ -phase rate constant for plasma decay (plasma assays) was .0155 min<sup>-1</sup>. The mean  $\beta$ -phase rate constant for plasma decay (plasma assays) was .0046 min<sup>-1</sup>; the mean  $\beta$ -phase rate constant for plasma decay (urine assays) was .0056 min<sup>-1</sup>. The mean  $\gamma$ -phase rate constant for plasma decay (urine assays) was .00075 min<sup>-1</sup>. These data demonstrate the existence of a third, deep, distribution compartment from which promazine is released slowly and which is only detectable by means of excretion studies.

L20 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:15911 HCAPLUS

DOCUMENT NUMBER: 112:15911

TITLE: Stability, human blood distribution and rat tissue localization of promazine and desmonomethylpromazine

AUTHOR(S): Hu, Oliver Y. P.; Curry, Stephen H.

CORPORATE SOURCE: Sch. Pharm., Natl. Def. Med. Cent., Taipei, Taiwan

SOURCE: Biopharmaceutics & Drug Disposition (1989), 10(6), 537-48

CODEN: BDDID8; ISSN: 0142-2782

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The stability in human blood and urine, partitioning into red blood cells, and plasma protein binding of promazine and desmonomethylpromazine were investigated. Tissue localization was investigated in rats. Promazine and desmonomethylpromazine were stable in human plasma and urine for at least 64 days at -20°. The percentage of promazine not bound to protein in plasma was 10.4% as estimated by equilibrium dialysis with correction for volume shift, and 11.6% as estimated by ultracentrifugation. Data for the mean plasma/red blood cell concentration ratio and the red blood cell/plasma distribution coefficient for promazine were 1.19 and 8.21, resp. There was no evidence of time-dependence in plasma/red blood cell partitioning. Ten rat organs and tissues were examined. The concns. of promazine and desmonemethylpromazine were highest in the lung. For promazine, the rank order of tissue localization was lung > liver > kidney > intestine > brain > spleen > red blood cell > skeletal muscle > plasma > stomach > heart. For desmonomethylpromazine, the order was reversed in the cases of spleen and brain and interchanged in the cases of stomach and muscle. The brain/plasma concentration ratios for promazine and desmonomethylpromazine in rat were 4.69 and 3.87, resp.

L20 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:193076 HCAPLUS

DOCUMENT NUMBER: 104:193076

TITLE: Relative bioavailability of trimeprazine tablets investigated in man using HPLC with electrochemical detection

AUTHOR(S): Hu, Oliver Y. P.; Gfeller, Edward; Perrin, John H.; Curry, Stephen H.

CORPORATE SOURCE: Coll. Pharm., Univ. Florida, Gainesville, FL, 32610, USA

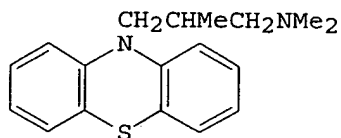
SOURCE: Journal of Pharmacy and Pharmacology (1986), 38(3), 172-6

CODEN: JPPMAB; ISSN: 0022-3573

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The stability, partition coefficient, plasma protein binding, red blood cell distribution, and whole blood concns. of trimeprazine (I) [84-96-8] were investigated. I solution was stable for 6 mo at -20° and 3.5 mo at 40°. In whole blood, I was stable for 5 wk at -20°, 24 h at 4°, 4 h at 25° and 1 h at 37°. The apparent hexane [110-54-3]-water partition coefficient varied from 1.50 (at pH 4.83) to over 100 (at pH 10.54). The fraction bound to plasma protein exceeded 0.9 as estimated by equilibrium dialysis with correction for volume shift. The mean plasma/red blood cell concentration ratio was 1.17 and the mean red blood cell/plasma distribution coefficient was 8.65. Six healthy adult males received single 5 mg dose of I in a syrup (5 mg in 10 mL) and tablets with at least 2 wk between doses. Blood was collected for 48 h. The mean

times for peak blood concns. were 3.5 and 4.5 h for syrup and tablets, resp. There were no significant differences in maximum blood concentration values.

The overall mean terminal phase half-life was 4.78 h. Mean areas under the concentration-time curves from 0 to infinity were 11.0 and 7.67 ng h<sup>-1</sup> mL<sup>-1</sup> for syrup and tablets, resp. The mean relative bioavailability for the tablets was .apprx.70% with respect to the syrup.

L20 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:125016 HCAPLUS

DOCUMENT NUMBER: 102:125016

TITLE: Evaluation of equilibrium dialysis volume shifts: a comment

AUTHOR(S): Curry, Stephen H.; Hu, Oliver Y. P.

CORPORATE SOURCE: Coll. Pharm., Univ. Florida, Gainesville, FL, 32610, USA

SOURCE: Journal of Pharmacokinetics and Biopharmaceutics (1984), 12(4), 463-5

CODEN: JPBPBJ; ISSN: 0090-466X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A polemic. The equation presented by J. J. Lima et al. (ibid. 1983, 11, 483-498) defining the fractional shift in volume (fs) as a general equation applicable to a wide variety of drug-protein binding situations during equilibrium dialysis actually applies only when the starting vols. before dialysis are equal. A better general definition is given by fs (volume shift)/(starting volume of protein solution).

L20 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:574326 HCAPLUS

DOCUMENT NUMBER: 97:174326

TITLE: Liquid chromatographic assay of phenothiazine, thioxanthene and butyrophenone neuroleptics and antihistamines in blood and plasma with conventional and radial compression columns and UV and electrochemical detection

AUTHOR(S): Curry, Stephen H.; Brown, Edgar A.; Hu, Oliver Y. P.; Perrin, John H.

CORPORATE SOURCE: Coll. Pharm., Univ. Florida, Gainesville, FL, 32610, USA

SOURCE: Journal of Chromatography (1982), 231(2), 361-76

CODEN: JOCRAM; ISSN: 0021-9673

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An assay strategy for determining a wide range of phenothiazine, thioxanthene and butyrophenone neuroleptics and antihistamines both alone and in combination in blood and plasma is described. The general method employs liquid chromatog. with both conventional and radial compression nitrile bonded columns. Detection is by UV absorption spectrophotometry or by amperometry depending on the concns. to be measured. UV absorption is suitable down to 10 ng/mL. Below this level amperometry is preferable. The various compds. are used as internal stds. for each other. The lower limit of detection is approx. 0.1ng/mL with a 10-mL sample. The within-run coefficient of variation is a maximum of 7.3%. The techniques were applied to clin. samples from patients treated with chlorpromazine [50-53-3], thioridazine [50-52-2], trifluoperazine [117-89-5], amitriptyline [50-48-6], or trimeprazine [84-96-8]. Some of the drug metabolites were also identified.

Spiyack 10\_080043- - Inventor Search

=> => d stat que l21

L20 19 SEA FILE=HCAPLUS ABB=ON PLU=ON YOA PU HU O/AU OR YOA PU HU OLIVER/AU OR HU O Y P/AU OR HU O YOA PU/AU OR HU OLIVER O Y/AU OR HU OLIVER Y P/AU

L21 13 SEA FILE=HCAPLUS ABB=ON PLU=ON (HSIONG C H/AU OR HSIONG CHENG HUEI/AU) NOT L20

=>

=>

=> d ibib abs l21 1-13

L21 ANSWER 1 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:558680 HCAPLUS

DOCUMENT NUMBER: 145:42754

TITLE: The method of blood sample for liver function test and the sample paper

INVENTOR(S): Hsiong, Cheng-Huei; Hsueh, Meng-Chuan; Pao, Li-Heng; Hu, Oliver Yoa-Pu

PATENT ASSIGNEE(S): Jacov Biotech Co., Peop. Rep. China

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060936	A1	20060615	WO 2004-CN1434	20041210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CN 1786683	A	20060614	CN 2004-10098444	20041210
			WO 2004-CN1434	A 20041210

PRIORITY APPLN. INFO.:

AB A method of blood sample preparation for liver function test and the sample paper is disclosed here. The method according to this invention comprises: inject a kind of galactose composition into a subject; take proper quantities of the subject's blood to drop on a filter paper for drying in shade after a time interval; solute the blood from the filter paper by trichloroacetic acid, and solute the blood by a kind of enzyme, to prepare a blood test sample, then analyze the concentration of galactose in the blood test

sample by micro-disk analyzer.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 2 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:301740 HCAPLUS

DOCUMENT NUMBER: 144:324786

TITLE: Cytochrome P450 2C9 inhibitors

INVENTOR(S): Hu, Oliver Yoa-Pu; Wang, Hong-Jaan; Hsiong, Cheng-Huei; Pao, Li-Heng  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S. Pat. Appl. Publ., 15 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006069042	A1	20060330	US 2004-948206	20040924
PRIORITY APPLN. INFO.:			US 2004-948206	20040924

AB This invention is to provide multiple specific inhibitors of cytochrome P 450 isoenzyme CYP2C9. These inhibitors can be derived from any combinations with the following compds. including: Tamarixetin, Formononetin, isoliquiritigenin, Phloretin, luteolin, Quercitrin, quercetin, myricetin, Wongonin, Puerarin, Genistein, Nordihydroguaiaretic acid, Narigenin, Capillarisin, Chrysin, Fisetin, eriodictyol, 6-Gingerol, Isorhamnetin, isoquercitrin, Morin, (+)-Taxifolin, isovitexin, 3-Phenylpropyl Acetate, Oleanolic acid, ursolic acid,  $\beta$ -Myrcene, cinnamic acid, Luteolin-7-Glucoside, Liquiritin, (+)Limonene, Homoorientin, Swertiamarin, Embelin, Daidzein, Poncirin, (-)-Epicatechin, ergosterol. These natural products can be used to enhance the bioavailability of therapeutic agents (drugs).

L21 ANSWER 3 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:164629 HCAPLUS  
 DOCUMENT NUMBER: 144:239871  
 TITLE: Inhibitors and enhancers of uridine diphosphate-glucuronosyltransferase 2b (ugt2b)  
 INVENTOR(S): Oliver, Yoa-Pu Hu; Hsiong, Cheng-Huei; Wang, Mei-Ting; Pao, Li-Heng  
 PATENT ASSIGNEE(S): National Defense Medical Center, Taiwan; National Defense University  
 SOURCE: U.S. Pat. Appl. Publ., 27 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006040875	A1	20060223	US 2005-28615	20050105
WO 2006072203	A1	20060713	WO 2005-CN2167	20051213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: TW 2004-93100465 A 20040128



US 2005-28615

A 20050105

AB A UGT2B inhibitor capable of increasing the bioavailability of a drug, being a compound in a free base or a pharmaceutically acceptable salt form that is selected from the group consisting of: capillarisin, isorhamnetin,  $\beta$ -naphthoflavone,  $\alpha$ -naphthoflavone, hesperetin, terpineol, (+)-limonene,  $\beta$ -myrcene, swertiamarin, eriodictyol, cineole, apigenin, baicalin, ursolic acid, isovitexin, lauryl alc., puerarin, trans-cinnamaldehyde, 3-phenylpropyl acetate, isoliquiritigenin, paeoniflorin, gallic acid, genistein, glycyrrhizin, protocatechuic acid, Et myristate, umbelliferone, and a combination thereof. A UGT2B enhancer capable of enhancing the liver detoxification function in a subject, being a compound in a free base or a pharmaceutically acceptable salt form that is selected from the group consisting of: mordihydroguaiaretic acid, wogonin, trans-cinnamic acid, baicalein, quercetin, daidzein, oleanolic acid, homoorientin, hesperetin, narigin, neohesperidin, (+) epicatechin, hesperidin, liquiritin, eriodictyol, formononetin, quercitrin, genkwanin, kaempferol, isoquercitrin, (+)-catechin, naringenin, daidzin, (-)epicatechin, luteolin-7-glucoside, ergosterol, rutin, luteolin, Et myristate, apigenin, 3-phenylpropyl acetate, umbelliferone, glycyrrhizin, protocatechuic acid, poncirin, isovitexin, 6-gingerol, cineole, genistein, trans-cinnamaldehyde, and a combination thereof. Rat were administered with both 100 mg/Kg nalbuphine and 4 mg/Kg capillarisin orally. The T<sub>max</sub> and C<sub>max</sub> for nalurphin was 25 min, and 2582 ng/mL resp., as compared with 97 min and 79 ng/mL for the control group which did not receive capillarsisin.

L21 ANSWER 4 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:250342 HCAPLUS

DOCUMENT NUMBER: 143:90705

TITLE: In vitro and in vivo evaluation of the metabolism and pharmacokinetics of sebacoyl dinalbuphine

AUTHOR(S): Pao, Li-Heng; Hsiong, Cheng-Huei; Hu, Oliver

Yoa-Pu; Wang, Jhi-Jung; Ho, Shung-Tai

CORPORATE SOURCE: Pharmaceutical Research Institute, National Defense Medical Center, Taipei, Taiwan

SOURCE: Drug Metabolism and Disposition (2005), 33(3), 395-402  
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A diester prodrug of nalbuphine, sebacoyl dinalbuphine (SDN), and its long-acting formulation are currently being developed to prolong the duration of nalbuphine. A comparative in vitro hydrolysis study was conducted for SDN in rat, rabbit, dog, and human blood. Both SDN and nalbuphine in blood or plasma were measured by high-performance liquid chromatog. The hydrolysis rates of SDN in blood were ranked as follows: rat > rabbit > human > dog. The rapid formation of nalbuphine in the blood accounted for almost 100% of the prodrug, which supported the contention that nalbuphine is the major metabolite after SDN hydrolysis. The hydrolysis profiles of SDN were similar both in plasma and in red blood cells when compared in the blood. In vitro release results of SDN long-acting formulation showed that the rate-limited step of SDN hydrolysis to nalbuphine in blood is the penetration of SDN from oil into the blood. After i.v. administration of SDN in sesame oil into rats, nalbuphine quickly appeared in plasma and, thereafter, exhibited monoexponential decay. Pharmaceutical dosage forms affecting the drug disposition kinetics were demonstrated after i.v. administration. The AUC of nalbuphine was significantly higher and clearance was significantly lower, without changes in the t<sub>1/2</sub> of nalbuphine after i.v. dosing of SDN

in sesame oil when compared with that of i.v. dosing with nalbuphine HCl in rats. Overall, these results suggest that SDN fulfilled the original pro-soft drug design in which the prodrug can rapidly metabolize to nalbuphine, and no other unexpected compds. were apparent in the blood.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:328193 HCAPLUS

DOCUMENT NUMBER: 140:380415

TITLE: Pharmacokinetics and bioequivalence study of a generic desloratadine tablet formulation in healthy male volunteers

AUTHOR(S): Yeh, Geng-Chang; Deng, Shin-Tarng; Lo, Chin-Yi; Chiang, Pei-Shan; Hsiong, Cheng-Huei

CORPORATE SOURCE: Department of Pediatrics, Taipei Medical University Hospital and Graduate Institute of Medical Science, Taipei Medical University, Taipei, Taiwan

SOURCE: Arzneimittel Forschung (2004), 54(3), 166-170  
CODEN: ARZNAD; ISSN: 0004-4172

PUBLISHER: Editio Cantor Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetic profiles and relative bioavailability of desloratadine tablets from two different pharmaceutical manufacturers were carried out. A single oral dose (10 mg/2 tablets) of desloratadine was administered to 8 healthy young Chinese males in a completely double-blind cross-over design with a two-week washout period between each dose. Plasma samples were obtained before and at various appropriate intervals after dosing up to 120 h. The plasma concns. were then analyzed by a liquid chromatog./tandem mass spectrometric (LC/MS/MS) method. The limit of quantitation of this LC/MS/MS method was 0.05 ng/mL. The coeffs. of variation of the within-day and between-day calibration curves (n = 6) range from 0.05 ng/mL to 10 ng/mL and were less than 10 %. The accuracy of this method was verified. Values for the area under the plasma concentration-time curve (AUC), peak concentration (Cmax), time to peak concentration (Tmax), elimination rate constant, half-life, oral clearance were estimated and compared for each preparation. By ANOVA, 90 % confidence interval, Mann-Whitney test, and paired t-test, the two desloratadine products can be considered bioequivalent for both the extent and the rate of absorption.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:34508 HCAPLUS

DOCUMENT NUMBER: 140:245961

TITLE: Single-point plasma or urine dextromethorphan method for determining CYP3A activity

AUTHOR(S): Kuo, Benjamin Pei-chung; Hu, Oliver Yoa-pu; Hsiong, Cheng-huei; Pao, Li-heng; Chen, Ting-shien; Hung, Chi-feng

CORPORATE SOURCE: Graduate Institute of Life Sciences, National Defense Medical Center and Academy Sinica, Taipei, Taiwan

SOURCE: Biopharmaceutics & Drug Disposition (2003), 24(9), 367-373

CODEN: BDDID8; ISSN: 0142-2782

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dextromethorphan is used widely in vivo to phenotype the polymorphically expressed cytochrome P 450 (CYP) 2D6. Also dextromethorphan is N-demethylated in vivo to 3-methoxymorphinan by human CYP3A4/5. The metabolic ratio (MR) of dextromethorphan/3-methoxymorphinan in plasma, saliva and urinary were examined as a possible in vivo probe of CYP3A activity. In limited previous studies, 4 h urinary samples were collected for determining the MR. To evaluate the repeatability and validity of previously reported and other potential phenotyping methods, the MR from urine samples (at various intervals), from plasma and from saliva (at varying time points) were determined after repetitive single doses of immediate-release or repetitive multiple doses of controlled-release dextromethorphan preps. For the single-dose study, each of 12 subjects received 15 mg of immediate-release dextromethorphan in periods II and I, resp., with a 1 wk washout period. For the multiple dose study, each of 16 subjects received 60 mg controlled release dextromethorphan twice daily for 5 days in periods I and II, resp., with a 2 wk washout period. Dextromethorphan and 3-methoxymorphinan are assayed by high-performance liquid chromatog. In the single-dose study, all of the urine MR revealed good repeatabilities for the periods (paired t-test). The urine MR at any time interval of 0-6 h, 0-8 h and 0-12 h correlated significantly with the MR from 0-24 h urine ( $r > 0.8$ ,  $p < 0.05$ ). In the multiple-dose study, all MR revealed good repeatabilities for the two periods (paired t-test). The plasma MR at any time between 0.5 h and 12 h, the saliva MR at 12 h and the urine MR at any interval between 0-2 h, 0-4 h, 0-6 h, 0-8 h, 0-12 h and 0-24 h could predict the MR from AUCs. In conclusion, the urine sample as 0-6 h, 0-8 h or 0-12 h in the single immediate-release dose (15 mg) or in the multiple controlled-release dose (60 mg) procedure, the saliva sample at 12 h, the urine sample at 0-2 h, 0-4 h, 0-6 h, 0-8 h, 0-12 h, 0-24 h or all plasma-sampling points 0.5-12 h could be used as the dextromethorphan MR for determining the CYP3A activity.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:848136 HCAPLUS

DOCUMENT NUMBER: 140:156596

TITLE: Novel inhibition of cis/trans retinoic acid interconversion in biological fluids-an accurate method for determination of trans and 13-cis-retinoic acid in biological fluids

AUTHOR(S): Wang, Chao-Jih; Pao, Li-Heng; Hsiong, Cheng-Huei; Wu, Chih-Yuan; Whang-Peng, Jacqueline Jia-Kang; Hu, Oliver Yoa-Pu

CORPORATE SOURCE: National Defense Medical Center, Graduate Institute of Life Science, Taipei, Taiwan

SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 796(2), 283-291

CODEN: JCBAAI; ISSN: 1570-0232

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB All-trans retinoic acid (tRA, or tretinoin) can be metabolized through stereoisomerization to 13-cis-retinoic acid (13-cRA) in vivo. We have developed a simple, sensitive and accurate method for analyzing tRA and 13-cRA in plasma with the addition of N-ethylmaleimide (NEM) and Vitamin C (Vit. C) to prevent the interconversion of cis/trans retinoic acid. All-trans RA, 9-cRA, and 13-cRA were well separated from each other in plasma by using a C18 precolumn and a column with a gradient solvent system of

mobile phases A and B at a flow rate of 1.0 mL/min. In addition, thermal stability of tRA and cRA in plasma during the sample preparation under the temperature of 0 and 25 were studied. Our results showed that (1) the interconversion ratios (%) (cRA/tRA and tRA/cRA) were decreased with the addition of NEM and Vit. C and the min. concns. of NEM and Vit. C to inhibit the interconversion were 50 and 150  $\mu$ M, resp., (2) higher concns. of NEM and Vit. C were required to prevent the interconversion at higher temperature, (3) the precision and accuracy of calibration curve with various concentration of tRA (1-1000 ng/mL) and 13-cRA (5-800 ng/mL) in plasma showed good linearity ( $r^2=0.9992$  and  $0.9994$ ), and between-day errors expressed by coefficient of variation (CV, %) for tRA and 13-cRA which were both less than 5.6%, (4) the mean recovery of the analytes were 78-94% for tRA and 80-92% for 13-cRA at concentration range from 1 to 1000 ng/mL and 5 to 800 ng/mL, resp., and (5) the limit of quantitation of tRA and 13-cRA were 1 and 5 ng/mL, resp. In addition, the HPLC method had been successfully applied to the tRA pharmacokinetic study in two hepatoma patients after receiving 45 mg/m<sup>2</sup> per day orally. Thus, our results suggest that the HPLC method for analyzing tRA and 13-cRA in plasma with the addition of NEM and Vit. C is a simple, sensitive and accurate method.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:696527 HCAPLUS

DOCUMENT NUMBER: 139:207741

TITLE: Cytochrome p450 3A inhibitors and enhancers

INVENTOR(S): Hu, Oliver Yoa-pu; Hsiong, Cheng-huei; Kuo, Benjamin Pei-chung; Pao, Li-heng

PATENT ASSIGNEE(S): Taiwan

SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003166584	A1	20030904	US 2002-80043	20020222
PRIORITY APPLN. INFO.:			US 2002-80043	20020222

AB The present invention provides cytochrome P 450 3A (CYP3A) inhibitors and enhancers. Examples of the CYP3A inhibitors include free bases or pharmacol. acceptable salts of at least one of the following compds.:  $\alpha$ - and  $\beta$ -naphthoflavone, apigenin, baicalein,  $\beta$ -myrcene, catechin, 3-phenylpropyl acetate, formononetin, gallic acid, hesperetin, hesperidin, isoquercitrin, lauryl alc., luteolin, luteolin 7-glycoside, narigin, nordihydroguaiaretic acid, quercitrin, swertiamarin, terpineol, and trans-cinnamaldehyde. Examples of the CYP3A enhancers include free bases or pharmacol. acceptable salts of at least one of the following compds.: apigenin, formononetin, and luteolin-7-glycoside. The CYP3A inhibitors can be used, alone or co-administered with a drug, to improve the drug bioavailability. The CYP3A inhibitors can also be used as chemopreventors to prevent biotransformation of procarcinogenic compds. into carcinogens via CYP3A activity or for treatment of intestinal or hepatic cancer by inhibit the CYP3A activity. The CYP3A enhancers can be used to improve the enzymic activity of CYP3A so as to improve the biotransformation and degradation of active drugs or the substrates of CYP3A from the body. The CYP3A inhibitors and enhancers of the present invention are natural substances extracted from herbs and non-toxic.

L21 ANSWER 9 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:472997 HCAPLUS  
 DOCUMENT NUMBER: 139:26683  
 TITLE: Controlled-release pharmaceutical preparation containing nalbuphine and a process for preparing the same  
 INVENTOR(S): Hu, Oliver Yoa-Pu; Hsiong, Cheng-Huei  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S. Pat. Appl. Publ., 17 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003113372	A1	20030619	US 2001-991608	20011126
US 6680067	B2	20040120		

PRIORITY APPLN. INFO.: US 2001-991608 20011126

AB A controlled-release pharmaceutical preparation containing an oil suspension which

comprises an analgesic and an injectable oil. The analgesic is either a nalbuphine free base or a pharmaceutical salt of nalbuphine such as nalbuphine HCl. The injectable oil is preferably sesame oil. The oil suspension contains microparticles in the size range of 1 to 100  $\mu$ m, preferably less than 50  $\mu$ m, which is produced by treating the analgesic and injectable oil in an ultra high energy mixing equipment. The controlled-release preparation permits nalbuphine free base or nalbuphine HCl to have a longer duration of action in relieving pain, and allows the administration of lower doses. A process for preparing the injectable oil suspension is also disclosed.

L21 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:435314 HCAPLUS  
 DOCUMENT NUMBER: 139:12237  
 TITLE: Orally administered analgesic compositions containing nalbuphine  
 INVENTOR(S): Hu, Oliver Yoa-pu; Hsiong, Cheng-huei  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S. Pat. Appl. Publ., 6 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003105120	A1	20030605	US 2001-991948	20011126
US 6703398	B2	20040309		
US 2004171631	A1	20040902	US 2004-795232	20040309

PRIORITY APPLN. INFO.: US 2001-991948 A3 20011126

AB The present invention provides orally administered pharmaceutical compns. which contains an effective amount of free base or pharmaceutically acceptable salts of nalbuphine and/or nalbuphine ester, an oily substance, and a solubility-assisting agent. The oily substance is preferably sesame oil. The solubility-assisting agent is preferably benzyl benzoate. The pharmaceutical composition is useful as an analgesic. The compns. achieves a much higher bioavailability rate and yields much longer lasting effects on

nalbuphine than other nalbuphine products currently in the market.

L21 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:276734 HCAPLUS  
 DOCUMENT NUMBER: 138:292770  
 TITLE: Stable galactose injection solutions  
 INVENTOR(S): Hu, Oliver Yoa-pu; Hsiong, Cheng-huei  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S., 16 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6544954	B1	20030408	US 2002-76650	20020219
PRIORITY APPLN. INFO.:			US 2002-76650	20020219

AB The present invention provides stable galactose injection solns., which contain 1 to 50% by weight of galactose, 0.01 to 1 M of a buffer solution, and 0.01 to 5% of an antioxidant. The preferred buffer solution is citrate buffer. The preferred anti-oxidant is sodium bisulfite. The galactose injection solution of the present invention has a pH between 4.0 and 9.0 and is stable at 80° C. for at least 2 wk.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2002:463527 HCAPLUS  
 DOCUMENT NUMBER: 138:49345  
 TITLE: Pharmacokinetics and bioequivalent study of generic fluoxetine capsules preparation  
 AUTHOR(S): Pan, Ryh-Nan; Chen, Ting-Hsien; Huang, Christine Shu-Hui; Hsiong, Cheng-Huei  
 CORPORATE SOURCE: Taiwan Police College, Taipei, Taiwan, Peop. Rep. China  
 SOURCE: Yaowu Shipin Fenxi (2002), 10(1), 13-17  
 CODEN: YSFEEP; ISSN: 1021-9498  
 PUBLISHER: National Laboratories of Food and Drugs, Dep. of Health, Executive Yuan  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The pharmacokinetics and relative bioavailability of fluoxetine capsules manufactured by two different pharmaceutical factories were carried out. A multiple oral dose ((20 mg/cap) + 2/day + 13 day) of fluoxetine was administered in 8 healthy young Chinese males in a completely double-blind cross-over design with a two week washout period between each dose. Plasma samples were obtained before (three min. concns.) and at various appropriate intervals after last dosing up to 72 h. The plasma concns. were then analyzed by a HPLC method. The limit of quantitation of this HPLC method was 5 ng/mL. The coeffs. of variation of the within-day and between-day calibration curves (n = 6) range from 5 ng/mL to 500 ng/mL were less than 16 %, and the accuracy of this method was also verified. Values for the area under the plasma concentration-time curve at steady state (AUC), peak concentration (Cmax), time to peak concentration (Tmax), elimination rate constant, half-life, oral clearance were estimated and compared

Spivack 10\_080043- - Inventor Search

for each preparation By ANOVA, power anal., 90% confidence interval, and two one-sided tests, PROZAC and FLUOXETINE can be considered bioequivalent.

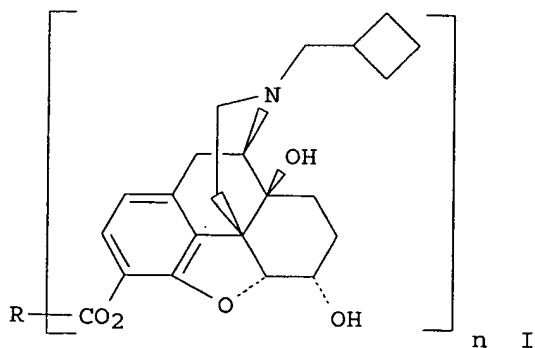
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:796281 HCAPLUS  
DOCUMENT NUMBER: 135:344630  
TITLE: Preparation of polynalbuphine derivatives  
INVENTOR(S): Hu, Oliver Yoa-Pu; Hsiong, Cheng-Huei  
PATENT ASSIGNEE(S): Taiwan  
SOURCE: Eur. Pat. Appl., 33 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1149836	A1	20011031	EP 2000-303532	20000427
EP 1149836	B1	20030226		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 233264	E	20030315	AT 2000-303532	20000427
ES 2188481	T3	20030701	ES 2000-303532	20000427
PRIORITY APPLN. INFO.:			EP 2000-303532	A 20000427
OTHER SOURCE(S):	MARPAT 135:344630			

GI



AB A polynalbuphine derivative I ( $n = \geq 2$ ; R is a substituted or unsubstituted C1-40 hydrocarbyl group) were prepared as pro drugs for the analgesic and narcotic antagonist nalbuphine. Thus, nalbuphine hydrochloride was treated with adipoyl chloride in  $\text{CH}_2\text{Cl}_2$  containing  $\text{Me}_3\text{N}$  to give adipoyl dinalbuphine ester. The release profiles of nalbuphine from I were determined. The pharmaceutical comps. comprising I suspended or dissolved in resp. oils and phosphate buffer were tested in animals such as dogs and Sprague Dawley rats for analgesic effect by i.m., i.v., and parenteral administration.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> => d stat que 122

Spivack - 10\_080043- - Inventor Search

L20 19 SEA FILE=HCAPLUS ABB=ON PLU=ON YOA PU HU O/AU OR YOA PU HU OLIVER/AU OR HU O Y P/AU OR HU O YOA PU/AU OR HU OLIVER O Y/AU OR HU OLIVER Y P?/AU

L21 13 SEA FILE=HCAPLUS ABB=ON PLU=ON (HSIONG C H/AU OR HSIONG CHENG HUEI/AU) NOT L20

L22 17 SEA FILE=HCAPLUS ABB=ON PLU=ON (KUO B/AU OR ("KUO BENJAMIN P"/AU OR "KUO BENJAMIN PEI CHUNG"/AU)) NOT L20 OR L21

=> d ibib abs hitstr l22 1-17

L22 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:558680 HCAPLUS

DOCUMENT NUMBER: 145:42754

TITLE: The method of blood sample for liver function test and the sample paper

INVENTOR(S): Hsiong, Cheng-Huei; Hsueh, Meng-Chuan; Pao, Li-Heng; Hu, Oliver Yoa-Pu

PATENT ASSIGNEE(S): Jacov Biotech Co., Peop. Rep. China

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006060936	A1	20060615	WO 2004-CN1434	20041210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
CN 1786683	A	20060614	CN 2004-10098444	20041210

PRIORITY APPLN. INFO.:

WO 2004-CN1434 A 20041210

AB A method of blood sample preparation for liver function test and the sample paper is disclosed here. The method according to this invention comprises: inject a kind of galactose composition into a subject; take proper quantities of the subject's blood to drop on a filter paper for drying in shade after a time interval; solute the blood from the filter paper by trichloroacetic acid, and solute the blood by a kind of enzyme, to prepare a blood test sample, then analyze the concentration of galactose in the blood test sample by micro-disk analyzer.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:301740 HCAPLUS

DOCUMENT NUMBER: 144:324786

TITLE: Cytochrome P450 2C9 inhibitors

INVENTOR(S): Hu, Oliver Yoa-Pu; Wang, Hong-Jaan; Hsiong, Cheng-Huei; Pao, Li-Heng



PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S. Pat. Appl. Publ., 15 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006069042	A1	20060330	US 2004-948206	20040924
PRIORITY APPLN. INFO.:			US 2004-948206	20040924

AB This invention is to provide multiple specific inhibitors of cytochrome P 450 isoenzyme CYP2C9. These inhibitors can be derived from any combinations with the following compds. including: Tamarixetin, Formononetin, isoliquiritigenin, Phloretin, luteolin, Quercitrin, quercetin, myricetin, Wongonin, Puerarin, Genistein, Nordihydroguaiaretic acid, Narigenin, Capillarisin, Chrysin, Fisetin, eriodictyol, 6-Gingerol, Isorhamnetin, isoquercitrin, Morin, (+)-Taxifolin, isovitexin, 3-Phenylpropyl Acetate, Oleanolic acid, ursolic acid,  $\beta$ -Myrcene, cinnamic acid, Luteolin-7-Glucoside, Liquiritin, (+)Limonene, Homoorientin, Swertiamarin, Embelin, Daidzein, Poncirin, (-)-Epicatechin, ergosterol. These natural products can be used to enhance the bioavailability of therapeutic agents (drugs).

L22 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:164629 HCAPLUS  
 DOCUMENT NUMBER: 144:239871  
 TITLE: Inhibitors and enhancers of uridine diphosphate-glucuronosyltransferase 2b (ugt2b)  
 INVENTOR(S): Oliver, Yoa-Pu Hu; Hsiong, Cheng-Huei; Wang, Mei-Ting; Pao, Li-Heng  
 PATENT ASSIGNEE(S): National Defense Medical Center, Taiwan; National Defense University  
 SOURCE: U.S. Pat. Appl. Publ., 27 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006040875	A1	20060223	US 2005-28615	20050105
WO 2006072203	A1	20060713	WO 2005-CN2167	20051213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: TW 2004-93100465 A 20040128  
 US 2005-28615 A 20050105  
 AB A UGT2B inhibitor capable of increasing the bioavailability of a drug,

being a compound in a free base or a pharmaceutically acceptable salt form that is selected from the group consisting of: capillarisin, isorhamnetin,  $\beta$ -naphthoflavone,  $\alpha$ -naphthoflavone, hesperetin, terpineol, (+)-limonene,  $\beta$ -myrcene, swertiamarin, eriodictyol, cineole, apigenin, baicalin, ursolic acid, isovitexin, lauryl alc., puerarin, trans-cinnamaldehyde, 3-phenylpropyl acetate, isoliquiritigenin, paeoniflorin, gallic acid, genistein, glycyrrhizin, protocathechuic acid, Et myristate, umbelliferone, and a combination thereof. A UGT2B enhancer capable of enhancing the liver detoxification function in a subject, being a compound in a free base or a pharmaceutically acceptable salt form that is selected from the group consisting of: mordihydroguaiaretic acid, wogonin, trans-cinnamic acid, baicalein, quercetin, daidzein, oleanolic acid, homoorientin, hesperetin, narigin, neohesperidin, (+) epicatechin, hesperidin, liquiritin, eriodictyol, formononetin, quercitrin, genkwanin, kaempferol, isoquercitrin, (+)-catechin, naringenin, daidzin, (-)epicatechin, luteolin-7-glucoside, ergosterol, rutin, luteolin, Et myristate, apigenin, 3-phenylpropyl acetate, umbelliferone, glycyrrhizin, protocathechuic acid, poncirin, isovitexin, 6-gingerol, cineole, genistein, trans-cinnamaldehyde, and a combination thereof. Rat were administered with both 100 mg/Kg nalbuphine and 4 mg/Kg capillarisin orally. The Tmax and Cmax for nalurphin was 25 min, and 2582 ng/mL resp., as compared with 97 min and 79 ng/mL for the control group which did not receive capillarsisin.

L22 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:250342 HCAPLUS

DOCUMENT NUMBER: 143:90705

TITLE: In vitro and in vivo evaluation of the metabolism and pharmacokinetics of sebacoyl dinalbuphine

AUTHOR(S): Pao, Li-Heng; Hsiong, Cheng-Huei; Hu, Oliver  
Yoa-Pu; Wang, Jhi-Jung; Ho, Shung-Tai

CORPORATE SOURCE: Pharmaceutical Research Institute, National Defense  
Medical Center, Taipei, Taiwan

SOURCE: Drug Metabolism and Disposition (2005), 33(3), 395-402  
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental  
Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A diester prodrug of nalbuphine, sebacoyl dinalbuphine (SDN), and its long-acting formulation are currently being developed to prolong the duration of nalbuphine. A comparative in vitro hydrolysis study was conducted for SDN in rat, rabbit, dog, and human blood. Both SDN and nalbuphine in blood or plasma were measured by high-performance liquid chromatog. The hydrolysis rates of SDN in blood were ranked as follows: rat > rabbit > human > dog. The rapid formation of nalbuphine in the blood accounted for almost 100% of the prodrug, which supported the contention that nalbuphine is the major metabolite after SDN hydrolysis. The hydrolysis profiles of SDN were similar both in plasma and in red blood cells when compared in the blood. In vitro release results of SDN long-acting formulation showed that the rate-limited step of SDN hydrolysis to nalbuphine in blood is the penetration of SDN from oil into the blood. After i.v. administration of SDN in sesame oil into rats, nalbuphine quickly appeared in plasma and, thereafter, exhibited monoexponential decay. Pharmaceutical dosage forms affecting the drug disposition kinetics were demonstrated after i.v. administration. The AUC of nalbuphine was significantly higher and clearance was significantly lower, without changes in the  $t_{1/2}$  of nalbuphine after i.v. dosing of SDN in sesame oil when compared with that of i.v. dosing with nalbuphine HCl in rats. Overall, these results suggest that SDN fulfilled the original

pro-soft drug design in which the prodrug can rapidly metabolize to nalbuphine, and no other unexpected compds. were apparent in the blood.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:328193 HCAPLUS

DOCUMENT NUMBER: 140:380415

TITLE: Pharmacokinetics and bioequivalence study of a generic desloratadine tablet formulation in healthy male volunteers

AUTHOR(S): Yeh, Geng-Chang; Deng, Shin-Tarng; Lo, Chin-Yi; Chiang, Pei-Shan; Hsiong, Cheng-Huei

CORPORATE SOURCE: Department of Pediatrics, Taipei Medical University Hospital and Graduate Institute of Medical Science, Taipei Medical University, Taipei, Taiwan

SOURCE: Arzneimittel Forschung (2004), 54(3), 166-170

CODEN: ARZNAD; ISSN: 0004-4172

PUBLISHER: Editio Cantor Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetic profiles and relative bioavailability of desloratadine tablets from two different pharmaceutical manufacturers were carried out. A single oral dose (10 mg/2 tablets) of desloratadine was administered to 8 healthy young Chinese males in a completely double-blind cross-over design with a two-week washout period between each dose. Plasma samples were obtained before and at various appropriate intervals after dosing up to 120 h. The plasma concns. were then analyzed by a liquid chromatog./tandem mass spectrometric (LC/MS/MS) method. The limit of quantitation of this LC/MS/MS method was 0.05 ng/mL. The coeffs. of variation of the within-day and between-day calibration curves (n = 6) range from 0.05 ng/mL to 10 ng/mL and were less than 10 %. The accuracy of this method was verified. Values for the area under the plasma concentration-time curve (AUC), peak concentration (Cmax), time to peak concentration (Tmax),

elimination rate constant, half-life, oral clearance were estimated and compared

for each preparation By ANOVA, 90 % confidence interval, Mann-Whitney test, and paired t-test, the two desloratadine products can be considered bioequivalent for both the extent and the rate of absorption.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:34508 HCAPLUS

DOCUMENT NUMBER: 140:245961

TITLE: Single-point plasma or urine dextromethorphan method for determining CYP3A activity

AUTHOR(S): Kuo, Benjamin Pei-chung; Hu, Oliver Yoa-pu; Hsiong, Cheng-huei; Pao, Li-heng; Chen, Ting-shien; Hung, Chi-feng

CORPORATE SOURCE: Graduate Institute of Life Sciences, National Defense Medical Center and Academy Sinica, Taipei, Taiwan

SOURCE: Biopharmaceutics & Drug Disposition (2003), 24(9), 367-373

CODEN: BDDID8; ISSN: 0142-2782

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dextromethorphan is used widely in vivo to phenotype the polymorphically

expressed cytochrome P 450 (CYP) 2D6. Also dextromethorphan is N-demethylated in vivo to 3-methoxymorphinan by human CYP3A4/5. The metabolic ratio (MR) of dextromethorphan/3-methoxymorphinan in plasma, saliva and urinary were examined as a possible in vivo probe of CYP3A activity. In limited previous studies, 4 h urinary samples were collected for determining the MR. To evaluate the repeatability and validity of previously reported and other potential phenotyping methods, the MR from urine samples (at various intervals), from plasma and from saliva (at varying time points) were determined after repetitive single doses of immediate-release or repetitive multiple doses of controlled-release dextromethorphan preps. For the single-dose study, each of 12 subjects received 15 mg of immediate-release dextromethorphan in periods II and I, resp., with a 1 wk washout period. For the multiple dose study, each of 16 subjects received 60 mg controlled release dextromethorphan twice daily for 5 days in periods I and II, resp., with a 2 wk washout period. Dextromethorphan and 3-methoxymorphinan are assayed by high-performance liquid chromatog. In the single-dose study, all of the urine MR revealed good repeatabilities for the periods (paired t-test). The urine MR at any time interval of 0-6 h, 0-8 h and 0-12 h correlated significantly with the MR from 0-24 h urine ( $r > 0.8$ ,  $p < 0.05$ ). In the multiple-dose study, all MR revealed good repeatabilities for the two periods (paired t-test). The plasma MR at any time between 0.5 h and 12 h, the saliva MR at 12 h and the urine MR at any interval between 0-2 h, 0-4 h, 0-6 h, 0-8 h, 0-12 h and 0-24 h could predict the MR from AUC<sub>ss</sub>. In conclusion, the urine sample as 0-6 h, 0-8 h or 0-12 h in the single immediate-release dose (15 mg) or in the multiple controlled-release dose (60 mg) procedure, the saliva sample at 12 h, the urine sample at 0-2 h, 0-4 h, 0-6 h, 0-8 h, 0-12 h, 0-24 h or all plasma-sampling points 0.5-12 h could be used as the dextromethorphan MR for determining the CYP3A activity.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:848136 HCAPLUS

DOCUMENT NUMBER: 140:156596

TITLE: Novel inhibition of cis/trans retinoic acid interconversion in biological fluids-an accurate method for determination of trans and 13-cis-retinoic acid in biological fluids

AUTHOR(S): Wang, Chao-Jih; Pao, Li-Heng; Hsiong, Cheng-Huei; Wu, Chih-Yuan; Whang-Peng, Jacqueline Jia-Kang; Hu, Oliver Yoa-Pu

CORPORATE SOURCE: National Defense Medical Center, Graduate Institute of Life Science, Taipei, Taiwan

SOURCE: Journal of Chromatography, B: Analytical Technologies in the Biomedical and Life Sciences (2003), 796(2), 283-291

CODEN: JCBAAI; ISSN: 1570-0232

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB All-trans retinoic acid (tRA, or tretinoin) can be metabolized through stereoisomerization to 13-cis-retinoic acid (13-cRA) in vivo. We have developed a simple, sensitive and accurate method for analyzing tRA and 13-cRA in plasma with the addition of N-ethylmaleimide (NEM) and Vitamin C (Vit. C) to prevent the interconversion of cis/trans retinoic acid. All-trans RA, 9-cRA, and 13-cRA were well separated from each other in plasma by using a C18 precolumn and a column with a gradient solvent system of mobile phases A and B at a flow rate of 1.0 mL/min. In addition, thermal stability of tRA and cRA in plasma during the sample preparation under the

temperature of 0 and 25 were studied. Our results showed that (1) the interconversion ratios (%) (cRA/tRA and tRA/cRA) were decreased with the addition of NEM and Vit. C and the min. concns. of NEM and Vit. C to inhibit the interconversion were 50 and 150  $\mu$ M, resp., (2) higher concns. of NEM and Vit. C were required to prevent the interconversion at higher temperature, (3) the precision and accuracy of calibration curve with various concentration of tRA (1-1000 ng/mL) and 13-cRA (5-800 ng/mL) in plasma showed good linearity ( $r^2=0.9992$  and  $0.9994$ ), and between-day errors expressed by coefficient of variation (CV, %) for tRA and 13-cRA which were both less than 5.6%, (4) the mean recovery of the analytes were 78-94% for tRA and 80-92% for 13-cRA at concentration range from 1 to 1000 ng/mL and 5 to 800 ng/mL, resp., and (5) the limit of quantitation of tRA and 13-cRA were 1 and 5 ng/mL, resp. In addition, the HPLC method had been successfully applied to the tRA pharmacokinetic study in two hepatoma patients after receiving 45 mg/m<sup>2</sup> per day orally. Thus, our results suggest that the HPLC method for analyzing tRA and 13-cRA in plasma with the addition of NEM and Vit. C is a simple, sensitive and accurate method.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:696527 HCAPLUS  
DOCUMENT NUMBER: 139:207741  
TITLE: Cytochrome p450 3A inhibitors and enhancers  
INVENTOR(S): Hu, Oliver Yoa-pu; Hsiong, Cheng-huei;  
Kuo, Benjamin Pei-chung; Pao, Li-heng  
PATENT ASSIGNEE(S): Taiwan  
SOURCE: U.S. Pat. Appl. Publ., 10 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003166584	A1	20030904	US 2002-80043	20020222

PRIORITY APPLN. INFO.: US 2002-80043 20020222

AB The present invention provides cytochrome P 450 3A (CYP3A) inhibitors and enhancers. Examples of the CYP3A inhibitors include free bases or pharmacol. acceptable salts of at least one of the following compds.:  $\alpha$ - and  $\beta$ -naphthoflavone, apigenin, baicalein,  $\beta$ -myrcene, catechin, 3-phenylpropyl acetate, formononetin, gallic acid, hesperetin, hesperidin, isoquercitrin, lauryl alc., luteolin, luteolin 7-glycoside, narigin, nordihydroguaiaretic acid, quercitrin, swertiamarin, terpineol, and trans-cinnamaldehyde. Examples of the CYP3A enhancers include free bases or pharmacol. acceptable salts of at least one of the following compds.: apigenin, formononetin, and luteolin-7-glycoside. The CYP3A inhibitors can be used, alone or co-administered with a drug, to improve the drug bioavailability. The CYP3A inhibitors can also be used as chemopreventors to prevent biotransformation of procarcinogenic compds. into carcinogens via CYP3A activity or for treatment of intestinal or hepatic cancer by inhibit the CYP3A activity. The CYP3A enhancers can be used to improve the enzymic activity of CYP3A so as to improve the biotransformation and degradation of active drugs or the substrates of CYP3A from the body. The CYP3A inhibitors and enhancers of the present invention are natural substances extracted from herbs and non-toxic.

L22 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2003:472997 HCAPLUS

DOCUMENT NUMBER: 139:26683  
 TITLE: Controlled-release pharmaceutical preparation containing nalbuphine and a process for preparing the same  
 INVENTOR(S): Hu, Oliver Yoa-Pu; Hsiong, Cheng-Huei  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S. Pat. Appl. Publ., 17 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003113372	A1	20030619	US 2001-991608	20011126
US 6680067	B2	20040120		

PRIORITY APPLN. INFO.: US 2001-991608 20011126

AB A controlled-release pharmaceutical preparation containing an oil suspension which

comprises an analgesic and an injectable oil. The analgesic is either a nalbuphine free base or a pharmaceutical salt of nalbuphine such as nalbuphine HCl. The injectable oil is preferably sesame oil. The oil suspension contains microparticles in the size range of 1 to 100  $\mu$ m, preferably less than 50  $\mu$ m, which is produced by treating the analgesic and injectable oil in an ultra high energy mixing equipment. The controlled-release preparation permits nalbuphine free base or nalbuphine HCl to have a longer duration of action in relieving pain, and allows the administration of lower doses. A process for preparing the injectable oil suspension is also disclosed.

L22 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:435314 HCAPLUS  
 DOCUMENT NUMBER: 139:12237  
 TITLE: Orally administered analgesic compositions containing nalbuphine  
 INVENTOR(S): Hu, Oliver Yoa-pu; Hsiong, Cheng-huei  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S. Pat. Appl. Publ., 6 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003105120	A1	20030605	US 2001-991948	20011126
US 6703398	B2	20040309		
US 2004171631	A1	20040902	US 2004-795232	20040309

PRIORITY APPLN. INFO.: US 2001-991948 A3 20011126

AB The present invention provides orally administered pharmaceutical compns. which contains an effective amount of free base or pharmaceutically acceptable salts of nalbuphine and/or nalbuphine ester, an oily substance, and a solubility-assisting agent. The oily substance is preferably sesame oil. The solubility-assisting agent is preferably benzyl benzoate. The pharmaceutical composition is useful as an analgesic. The compns. achieves a much higher bioavailability rate and yields much longer lasting effects on nalbuphine than other nalbuphine products currently in the market.

Spivack 10\_080043-- Inventor Search

L22 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:276734 HCAPLUS  
 DOCUMENT NUMBER: 138:292770  
 TITLE: Stable galactose injection solutions  
 INVENTOR(S): Hu, Oliver Yoa-pu; Hsiong, Cheng-huei  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S., 16 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6544954	B1	20030408	US 2002-76650	20020219
PRIORITY APPLN. INFO.:			US 2002-76650	20020219

AB The present invention provides stable galactose injection solns., which contain 1 to 50% by weight of galactose, 0.01 to 1 M of a buffer solution, and 0.01 to 5% of an antioxidant. The preferred buffer solution is citrate buffer. The preferred anti-oxidant is sodium bisulfite. The galactose injection solution of the present invention has a pH between 4.0 and 9.0 and is stable at 80° C. for at least 2 wk.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:96557 HCAPLUS  
 DOCUMENT NUMBER: 138:203224  
 TITLE: CMRF-35A, CMRF-35H: potential new CD  
 AUTHOR(S): Clark, G. J.; Fitzpatrick, S.; Kuo, B.;  
 Modra, C.; Jamrisk, L.; Hart, D. N. J.  
 CORPORATE SOURCE: Mater Medical Research Institute, South Brisbane,  
 Australia  
 SOURCE: Journal of Biological Regulators and Homeostatic  
 Agents (2002), 16(3), 233-235  
 CODEN: JBRAER; ISSN: 0393-974X  
 PUBLISHER: Wichtig Editore  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 AB A review discussing the structure, cell and tissue distribution, and  
 function of CMRF-35H and CMRF-35A.  
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2002:463527 HCAPLUS  
 DOCUMENT NUMBER: 138:49345  
 TITLE: Pharmacokinetics and bioequivalent study of generic  
 fluoxetine capsules preparation  
 AUTHOR(S): Pan, Ryh-Nan; Chen, Ting-Hsien; Huang, Christine  
 Shu-Hui; Hsiong, Cheng-Huei  
 CORPORATE SOURCE: Taiwan Police College, Taipei, Taiwan, Peop. Rep.  
 China  
 SOURCE: Yaowu Shipin Fenxi (2002), 10(1), 13-17  
 CODEN: YSFEEP; ISSN: 1021-9498  
 PUBLISHER: National Laboratories of Food and Drugs, Dep. of  
 Health, Executive Yuan  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The pharmacokinetics and relative bioavailability of fluoxetine capsules manufactured by two different pharmaceutical factories were carried out. A multiple oral dose ((20 mg/cap) + 2/day + 13 day) of fluoxetine was administered in 8 healthy young Chinese males in a completely double-blind cross-over design with a two week washout period between each dose. Plasma samples were obtained before (three min. concns.) and at various appropriate intervals after last dosing up to 72 h. The plasma concns. were then analyzed by a HPLC method. The limit of quantitation of this HPLC method was 5 ng/mL. The coeffs. of variation of the within-day and between-day calibration curves (n = 6) range from 5 ng/mL to 500 ng/mL were less than 16 %, and the accuracy of this method was also verified. Values for the area under the plasma concentration-time curve at steady state (AUC), peak concentration (Cmax), time to peak concentration (Tmax), elimination rate constant, half-life, oral clearance were estimated and compared for each preparation. By ANOVA, power anal., 90% confidence interval, and two one-sided tests, PROZAC and FLUOXETINE can be considered bioequivalent.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:209139 HCAPLUS

DOCUMENT NUMBER: 137:226447

TITLE: Effects of 5-HT3 antagonism on postprandial gastric volume and symptoms in humans

AUTHOR(S): Kuo, B.; Camilleri, M.; Burton, D.; Viramontes, B.; McKinzie, S.; Thomforde, G.; O'Connor, M. K.; Brinkmann, B. H.

CORPORATE SOURCE: Gastroenterology Unit, Massachusetts General Hospital, Boston, MA, USA

SOURCE: Alimentary Pharmacology and Therapeutics (2002), 16(2), 225-233  
CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER: Blackwell Publishing Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of placebo and of the 5-HT3 antagonist alosetron (0.5 and 1 mg twice daily) on fasting and postprandial gastric vols. and symptoms were assessed in healthy volunteers 30 min after ingestion of the maximum tolerable volume of a liquid meal. The 5-HT3 antagonist reduced postprandial symptoms and nausea and tended to reduce bloating. Both 0.5 and 1 mg alosetron reduced nausea; 1 mg alosetron reduced aggregate symptoms and bloating. Effects on pain and feeling of fullness were not significant. There were no significant effects of the 5-HT3 antagonist on the volume of meal tolerated or on fasting or postprandial gastric vols. Ths, 5-HT3 antagonism reduces aggregate symptoms, nausea and bloating after a liquid meal without increase in gastric vols., suggesting a role for 5-HT3 receptors in afferent functions in healthy humans during the postprandial period.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:796281 HCAPLUS

DOCUMENT NUMBER: 135:344630

TITLE: Preparation of polynalbuphine derivatives

INVENTOR(S): Hu, Oliver Yoa-Pu; Hsiong, Cheng-Huei

PATENT ASSIGNEE(S): Taiwan



SOURCE: Eur. Pat. Appl., 33 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

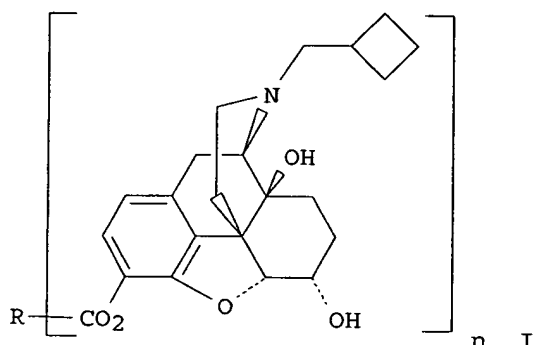
LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1149836	A1	20011031	EP 2000-303532	20000427
EP 1149836	B1	20030226		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 233264	E	20030315	AT 2000-303532	20000427
ES 2188481	T3	20030701	ES 2000-303532	20000427
PRIORITY APPLN. INFO.:			EP 2000-303532	A 20000427
OTHER SOURCE(S):	MARPAT 135:344630			
GI				



AB A polynalbuphine derivative I ( $n \geq 2$ ; R is a substituted or unsubstituted C1-40 hydrocarbyl group) were prepared as pro drugs for the analgesic and narcotic antagonist nalbuphine. Thus, nalbuphine hydrochloride was treated with adipoyl chloride in  $\text{CH}_2\text{Cl}_2$  containing  $\text{Me}_3\text{N}$  to give adipoyl dinalbuphine ester. The release profiles of nalbuphine from I were determined. The pharmaceutical compns. comprising I suspended or dissolved in resp. oils and phosphate buffer were tested in animals such as dogs and Sprague Dawley rats for analgesic effect by i.m., i.v., and parenteral administration.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:58972 HCAPLUS

DOCUMENT NUMBER: 130:276521

TITLE: Nocturnal gastric acidity and acid breakthrough on different regimens of omeprazole 40 mg daily

AUTHOR(S): Hatlebakk, J. G.; Katz, P. O.; Kuo, B.; Castell, D. O.

CORPORATE SOURCE: Esophageal Research Laboratory, Department of Medicine, Allegheny University Hospitals-Graduate, Philadelphia, PA, USA

SOURCE: Alimentary Pharmacology and Therapeutics (1998),

12(12), 1235-1240

CODEN: APTHEN; ISSN: 0269-2813

PUBLISHER:

Blackwell Science Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB Background: On chronic intake of omeprazole, most healthy volunteers and patients still have nocturnal acid breakthrough (NAB), defined as night-time periods with gastric pH <4.0 lasting for longer than 1 h. Gastro-esophageal reflux during NAB may be particularly injurious to the esophageal mucosa, contributing to the chronic lesions complicating the condition. Aim: To compare the effect of 3 different dosing regimens of omeprazole 40 mg daily with regard to suppressing nocturnal gastric acidity and avoiding NAB. Methods: Eighteen healthy volunteers were given 3 different regimens of omeprazole for 7 days each in randomized order: 40 mg before breakfast (qAM), 40 mg before dinner (qPM), and 20 mg before breakfast and dinner (b.d.). On day 7, 24-h intragastric and intra-esophageal pH-metry was performed. Tracings were analyzed for the period from 22.00 h until 06.00 h with regard to the percentage of time at which gastric pH was below 4.0, 3.0, and 2.0, and also the occurrence and duration of NAB. Results: Nocturnal acid breakthrough was significantly more common on qAM than on qPM and b.d. ( $P < 0.05$ ) dosing. The percentage of time gastric pH was <4.0 overnight was significantly lower on qPM (median 31.3) and b.d. (median 20.5) than on qAM (median 66.3) dosing ( $P = 0.01$  and  $P < 0.02$ , resp.). A pH threshold of 3 and 4 showed the same differences, as did median 24-h gastric pH. Daytime acidity was not significantly different. Conclusions: In healthy volunteers, dinner time or split dosing of omeprazole 40 mg daily is significantly more effective than dosing before breakfast in preventing NAB and controlling gastric acidity. These regimens should be preferred in patients in whom suppression of nocturnal gastric acidity is desirable.

REFERENCE COUNT:

27

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:

1995:935847 HCAPLUS

DOCUMENT NUMBER:

124:14693

TITLE:

Effectiveness of innovative technologies for treatment of hazardous soil

AUTHOR(S):

Weisman, Richard J.; Falatko, Stephen M.; Kuo, Benjamin P.; Eby, Elaine

CORPORATE SOURCE:

Radian Corporation, Herndon, VA, USA

SOURCE:

Proceedings, Annual Meeting - Air &amp; Waste Management Association (1994), 87th(Vol. 13, Hazardous Waste Management &amp; Control), 9 pp 94-TP62.04

CODEN: PAMEE5; ISSN: 1052-6102

PUBLISHER:

Air &amp; Waste Management Association

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB The contents of a USEPA database containing innovative technologies to remediate hazardous soils are summarized. Topics discussed include: effectiveness of innovative technologies to treat hazardous soil; proposed regulatory definitions; proposed treatment stds. for hazardous soils; soil treatability database; and effectiveness of innovative technologies. Innovative technologies considered include: bioslurry, chemical extraction, high-temperature metal recovery, soil washing, stabilization, and thermal desorption.

=&gt; =&gt; d stat que 123

L20

19 SEA FILE=HCAPLUS ABB=ON PLU=ON YOA PU HU O/AU OR YOA PU HU

Spivack 10\_080043- - Inventor Search

OLIVER/AU OR HU O Y P/AU OR HU O YOA PU/AU OR HU OLIVER O Y/AU  
OR HU OLIVER Y P?/AU

L21 13 SEA FILE=HCAPLUS ABB=ON PLU=ON (HSIONG C H/AU OR HSIONG  
CHENG HUEI/AU) NOT L20

L22 17 SEA FILE=HCAPLUS ABB=ON PLU=ON (KUO B/AU OR ("KUO BENJAMIN  
P"/AU OR "KUO BENJAMIN PEI CHUNG"/AU)) NOT L20 OR L21

L23 17 SEA FILE=HCAPLUS ABB=ON PLU=ON (PAO L/AU OR PAO L H/AU OR  
PAO LI HENG/AU OR PAO H/AU) NOT (L20 OR L21 OR L22)

=>

=>

=> d ibib abs l23 1-17

L23 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:188963 HCAPLUS

DOCUMENT NUMBER: 139:219421

TITLE: Applications of polyion-sensitive electrodes to  
pharmaceutical domain: a mini-review

AUTHOR(S): Lee, An-Rong; Chang, Li-Chien; Yang, Victor C.;  
Pao, Li-Heng; Wang, Da-Peng

CORPORATE SOURCE: School of Pharmacy, National Defense Medical Center,  
Taipei, 114, Taiwan

SOURCE: Yaowu Shipin Fenxi (2002), 10(4), 212-218

CODEN: YSFEEP; ISSN: 1021-9498

PUBLISHER: National Laboratories of Food and Drugs, Dep. of  
Health, Executive Yuan

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Recent development in the pharmaceutical applications of  
polyion-sensitive electrodes (PSEs) is reviewed. The general electrochem.  
principle governing the potentiometric response of such polymer  
membrane-based devices is summarized and applications for the use of these  
novel sensors are detailed. These new applications include methods to  
quantitate the anticoagulant heparin and pentosan polysulfate, an  
anti-osteoarthritis drug, via titration with polycationic protamine or  
polyarginine, as well as selective assay on fibrinolytic enzymes (e.g.,  
plasminogen activators and plasminogen) using protamine as the substrate  
based on potentiometric polyion detection.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:966925 HCAPLUS

DOCUMENT NUMBER: 139:159388

TITLE: Pharmacokinetic properties of tranilast in Chinese  
people

AUTHOR(S): Charng, Min-Ji; Ding, Philip Yu-An; Chuang, Mei-Hua;  
Lo, Chin-Yi; Chiang, Pei-Shan; Pao, Li-Heng

CORPORATE SOURCE: Division of Cardiology, Taipei Veterans General  
Hospital and National Yang-Ming University, Taipei,  
Peop. Rep. China

SOURCE: Yaowu Shipin Fenxi (2002), 10(3), 135-138

CODEN: YSFEEP; ISSN: 1021-9498

PUBLISHER: National Laboratories of Food and Drugs, Dep. of  
Health, Executive Yuan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The pharmacokinetics and relative bioavailability of two different

formulated tranilast capsules were determined after single dosing in twelve healthy Chinese subjects in a two-way crossover study. Blood samples were obtained from predose until 24 h postdose. Plasma concentration of tranilast

was

determined by an HPLC method. Since no differences in pharmacokinetic parameters were found between the two distinctive tranilast products (Tranpro and Rizaben), the data were pooled together to characterize the pharmacokinetic property of tranilast. Mean peak plasma concns. after dosing and the time at which it occurred (Tmax) were  $42.2 \pm 5.92$   $\mu\text{g/mL}$  and  $2.79 \pm 1.14$  h, resp. The elimination half-life and total body plasma clearance were  $7.58 \pm 1.44$  h and  $8.12 \pm 1.31$  mL/h/kg, resp. The resp. areas under the concentration-time curve from time 0 to infinity for Tranpro

and

Rizaben were  $431 \pm 97$  and  $412 \pm 60$   $\mu\text{g.h/mL}$ . The results also indicated that the two tranilast products can be considered as bioequivalent.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:48155 HCAPLUS

DOCUMENT NUMBER: 134:246852

TITLE: Regional-dependent intestinal absorption and meal composition effects on systemic availability of LY303366, a lipopeptide antifungal agent, in dogs  
AUTHOR(S): Li, C.; Fleisher, D.; Li, L.; Schwier, J. R.; Sweetana, S. A.; Vasudevan, V.; Zornes, L. L.; Pao, L-H.; Zhou, S. Y.; Stratford, R. E.

CORPORATE SOURCE: 3058 College of Pharmacy, University of Michigan, Ann Arbor, MI, 48109-1065, USA

SOURCE: Journal of Pharmaceutical Sciences (2001), 90(1), 47-57

CODEN: JPMSAE; ISSN: 0022-3549

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Low oral bioavailability and a neg. meal effect on drug plasma levels motivated studies on formulation and meal composition effects on the absorption of LY303366, a poorly water-soluble, semisynthetic, cyclic peptide antifungal drug. Solid drug particle size and meal composition studies were evaluated in beagle dogs. Canine regional absorption studies were also carried out utilizing surgically implanted intestinal access ports, and Caco-2 studies were performed to evaluate drug candidate intestinal permeability. Particle size and Caco-2 data indicate that drug permeability limitations to absorption are more important than dissoln. rate limits. Caco-2 cell-associated LY303366 approached 10% of incubation concentration that is in

the

range of the oral bioavailability of the drug. Canine regional absorption studies showed that the extent of LY303366 absorption following duodenal administration was similar to that following oral administration. Significantly lower drug plasma levels were obtained following administration through a colonic access port, a result consistent with poor membrane permeation. Administration of drug with meals of mixed composition, as well as simple fat and protein meals, resulted in significant redns. in AUC0-48h compared with results from fasted dogs. In contrast, carbohydrate meals did not reduce drug plasma levels compared to controls. I.v. pretreatment with devazepide, a cholecystokinin (CCK) antagonist that blocks canine biliary secretion, did not reverse the neg. effect of the fat meal on LY303366. Taken together, the results from the present study suggest that membrane-permeability-limited absorption is the cause of the

observed regionally dependent absorption of LY303366 in the dog and that the observed neg. meal effects depend on composition but are independent of biliary secretion.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:725329 HCAPLUS

DOCUMENT NUMBER: 132:44456

TITLE: Regulation of paracellular absorption of cimetidine and 5-aminosalicylate in rat intestine

AUTHOR(S): Zhou, Simon Yuji; Piyapolrungrroj, Nusara; Pao, Li-Heng; Li, Cheng; Liu, Guangyu; Zimmermann, Ellen; Fleisher, David

CORPORATE SOURCE: Candidate Synthesis Enhancement and Evaluation, Candidate Synthesis Enhancement and Evaluation, Pfizer Central Research, Groton, CT, 06340, USA

SOURCE: Pharmaceutical Research (1999), 16(11), 1781-1785

CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Kluwer Academic/Plenum Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Isolating the relative contributions of parallel transcellular and paracellular transport to the intestinal absorption of small hydrophilic mols. has proven exptl. challenging. In this report, luminal appearance of drug metabolite is utilized as a tool to assess the contribution of paracellular transport to the absorption of cimetidine and 5-aminosalicylate (5ASA) in rat small intestine. Steady-state intestinal absorption and elimination of cimetidine and 5ASA were studied in single-pass intestinal perfusions in rats. Both drugs were metabolized in intestinal epithelia with subsequent metabolite secretion into the intestinal lumen. Jejunal cimetidine absorption decreased with increasing perfusion concentration while the ratio of luminal metabolite to luminal drug loss increased. Cimetidine uptake at perfusion concns. above 0.4 mM resulted in over 80% drug elimination into the jejunal lumen. Inhibition of intracellular metabolism of cimetidine by methimazole did not alter epithelial uptake but totally abolished transepithelial cimetidine flux indicating an elevation of intracellular cimetidine. Similarly, co-perfusion of 5ASA with cimetidine and methimazole totally abolished 5ASA absorption but increased luminal levels of N-acetyl 5ASA indicating an increase in intracellular uptake of 5ASA. Conclusions. Cimetidine and 5ASA absorption across rat jejunal epithelia are exclusively paracellular. Elevation of intracellular cimetidine, inferred from mass balance considerations, restricts paracellular transport of both drugs.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:290851 HCAPLUS

DOCUMENT NUMBER: 131:110750

TITLE: Drug, meal and formulation interactions influencing drug absorption after oral administration: clinical implications

AUTHOR(S): Fleisher, David; Li, Cheng; Zhou, Yuji; Pao, Li-Heng; Karim, Aziz

CORPORATE SOURCE: College of Pharmacy, The University of Michigan, Ann Arbor, MI, USA

SOURCE: Clinical Pharmacokinetics (1999), 36(3), 233-254

CODEN: CPKNDH; ISSN: 0312-5963

PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 185 refs. Drug-drug, drug-formulation and drug-meal interactions are of clin. concern for orally administered drugs that possess a narrow therapeutic index. This review presents the current status of information regarding interactions which may influence the gastrointestinal (GI) absorption of orally administered drugs. Absorption interactions have been classified on the basis of rate-limiting processes. These processes are put in the context of drug and formulation physicochem. properties and oral input influences on variable GI physiol. Interaction categorization makes use of a biopharmaceutical classification system based on drug aqueous solubility and membrane permeability and their contributions towards absorption variability. Overlaying this classification it is important to be aware of the effect that the magnitudes of drug dosage and volume of fluid administration can have on interactions involving a solubility rate limits. GI regional differences in membrane permeability are fundamental to the rational development of extended release dosage forms as well as to predicting interaction effects on absorption from immediate release dosage forms. The effect of meals on the regional-dependent intestinal elimination of drugs and their involvement in drug absorption interactions is also discussed. Although the clin. significance of such interactions is certainly dependent on the narrowness of the drug therapeutic index, clin. aspects of absorption delays and therapeutic failures resulting from various interactions are also important.

REFERENCE COUNT: 187 THERE ARE 187 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:270257 HCAPLUS

DOCUMENT NUMBER: 131:39178

TITLE: Intestinal metabolism and transport of 5-aminosalicylate

AUTHOR(S): Zhou, S. Y.; Fleisher, D.; Pao, L. H.; Li, C.; Winward, B.; Zimmermann, E. M.

CORPORATE SOURCE: College of Pharmacy, The University of Michigan, Ann Arbor, MI, 48109-0586, USA

SOURCE: Drug Metabolism and Disposition (1999), 27(4), 479-485  
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: American Society for Pharmacology and Experimental Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of this study was to determine the characteristics of intestinal absorption and metabolism of 5-aminosalicylic acid (5ASA). Regional perfusions of 5ASA in the anesthetized rat resulted in the appearance of N-acetyl-5-aminosalicylic acid in the intestinal lumen. Luminal metabolite appearance was proportional to 5ASA permeability, which was 5-fold higher in the jejunum than in the ileum. Intestinal elimination significantly decreases 5ASA absorption at low luminal drug concns. and this process is saturated at high drug concns. Metabolite levels in intestinal tissue were higher than plasma levels at low perfusion drug concns., whereas the reverse was observed at high concns. Transport and metabolism of 5ASA was studied in Caco-2 monolayers. At low drug concns., 5ASA was preferentially transported in the basolateral (BL) to apical (AP) direction. With 5ASA incubation in either the AP or BL chamber, the N-acetyl metabolite appeared only in the AP compartment. Transport of N-acetyl-5-aminosalicylic acid was also exclusively observed in the BL to AP direction. Clin. data indicate that anti-inflammatory response to oral

5ASA correlates with the amount of 5ASA delivered to the intestinal tissue. This study shows that at luminal levels below 200 µg/mL (concns. that are typically achieved by controlled release dosage forms), intestinal secretion of 5ASA accounts for more than 50% of the total elimination and can significantly affect tissue levels and, therefore, may be an important factor in determining the response to 5ASA therapy.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:154456 HCAPLUS

DOCUMENT NUMBER: 128:265759

TITLE: Reduced systemic availability of an antiarrhythmic drug, bidisomide, with meal co-administration: relationship with region-dependent intestinal absorption

AUTHOR(S): Pao, Li-Heng; Zhou, Simon Yuji; Cook, Chyung; Kararli, Tugrul; Kirchhoff, Carol; Truelove, James; Karim, Aziz; Fleisher, David

CORPORATE SOURCE: College of Pharmacy, The University of Michigan, Ann Arbor, MI, 48109-1065, USA

SOURCE: Pharmaceutical Research (1998), 15(2), 221-227  
CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Plenum Publishing Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this research was to determine the mechanism by which a co-administered meal decreases the oral absorption of bidisomide and does not influence the oral absorption of the chemical-related antiarrhythmic agent, disopyramide. Bidisomide plasma levels, following oral administration and i.v. infusion in the fasted state and with various meal treatments, were determined in human subjects. A dialysis technique was employed to examine the potential for drug binding to meal homogenates. Plasma levels, following drug administration through duodenal and jejunal intestinal access ports and following various meal treatments with oral drug co-administration, were compared for bidisomide and disopyramide in a canine model. Bidisomide plasma AUC was significantly reduced following oral drug co-administration with breakfast compared to fasted-state controls in human subjects and in dogs independent of the composition of the solid cooked breakfast. While i.v. bidisomide infusion in human subjects showed a statistically significant reduction in AUC 15 min after oral administration of a high fat breakfast as compared to drug infusion in the fasted state, the reduction (-13%) was substantially smaller than the reduction (from -43% to -63%) observed with oral bidisomide meal co-administration. The percentages of bidisomide and disopyramide lost by binding to homogenates of cooked breakfast were  $25.0 \pm 5.7\%$  and  $23.7 \pm 7.7\%$ , resp., as determined by dialysis at 4 h. In dogs, the extent of absorption of disopyramide was comparable from oral, duodenal and mid-jejunal administration while the extent of bidisomide absorption from mid-jejunal administration was significantly lower than for oral or duodenal administration. Non-viscous liquid meals decreased Cmax but not AUC, while viscous homogenized solid meals decreased both Cmax and AUC for bidisomide with oral drug-meal co-administration. Oral non-caloric hydroxypropyl methylcellulose meals decreased bidisomide to the same extent as homogenized solid meals but did not lower disopyramide AUC. The significant reduction in bidisomide plasma levels observed with meal co-administration in human subjects was predominantly mediated through a reduction in drug absorption and was independent of solid meal composition. The difference in meal effect on the absorption of the two drugs in humans did not appear to be a function of drug binding to cooked meal components over

typical human upper gastrointestinal residence times. In dogs, the high-viscosity medium generated by oral co-administration of a solid meal reduced the upper intestinal absorption of bidisomide and disopyramide. Bidisomide AUC was decreased since it was well absorbed in the upper but not lower small intestine. Disopyramide AUC was not significantly affected since it was well absorbed from both regions. A similar mechanism may play a role in drug plasma level redns. following oral co-administration with solid meals for drugs showing similar regionally-dependent absorption profiles.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:152757 HCAPLUS  
DOCUMENT NUMBER: 128:175778  
TITLE: Effect of food on the absorption of drugs:  
relationship with site-specific absorption in dogs  
AUTHOR(S): Pao, Li-Heng  
CORPORATE SOURCE: Univ. of Michigan, Ann Arbor, MI, USA  
SOURCE: (1997) 133 pp. Avail.: UMI, Order No. DA9811153  
From: Diss. Abstr. Int., B 1998, 58(10), 5408  
DOCUMENT TYPE: Dissertation  
LANGUAGE: English  
AB Unavailable

L23 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:463872 HCAPLUS  
DOCUMENT NUMBER: 127:126489  
TITLE: Targeting drugs to the intestine with oral liposomes  
AUTHOR(S): Zhou, S. Y.; Pao, L. H.; Weiner, N.;  
Fleisher, D.; Zimmermann, E.  
CORPORATE SOURCE: College of pharmacy, The University of Michigan, Ann  
Arbor, MI, 48109, USA  
SOURCE: Proceedings of the International Symposium on  
Controlled Release of Bioactive Materials (1997),  
24th, 855-856  
CODEN: PCRMEY; ISSN: 1022-0178  
PUBLISHER: Controlled Release Society, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB 5-Aminosalicylic acid incorporated in liposomes and delivered resulted in decreased systemic absorption and altered kinetics of the drug metabolism, suggesting increased intestinal delivery and N-acetylation. The use of liposomes as drug delivery systems for the treatment of inflammatory bowel diseases is discussed.

L23 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:463448 HCAPLUS  
DOCUMENT NUMBER: 127:130418  
TITLE: Regional absorption and food effect in dogs  
AUTHOR(S): Pao, L.H.; Zhou, S.Y.; Medina, C.; Cook, C.;  
Fleisher, D.  
CORPORATE SOURCE: College of Pharmacy, University of Michigan, Ann  
Arbor, MI, 48109, USA  
SOURCE: Proceedings of the International Symposium on  
Controlled Release of Bioactive Materials (1997),  
24th, 9-10  
CODEN: PCRMEY; ISSN: 1022-0178  
PUBLISHER: Controlled Release Society, Inc.  
DOCUMENT TYPE: Journal



LANGUAGE: English

AB Regional absorption profiles between antiarrhythmic agents bidisomide and disopyramide was investigated through intestinal access port administration in dogs. In contrast to the consistent absorption along the small intestine for disopyramide, bidisomide is mainly absorbed in the duodenum of dogs despite the chemical similarity between drugs. The regional differences in absorption of bidisomide may play an important role in the observed food effect in dog.

L23 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:587056 HCAPLUS

DOCUMENT NUMBER: 121:187056

TITLE: HPLC assay for basic amine drug in plasma using a silica gel column and an aqueous mobile phase-application in a pilot bioavailability study of chlorpheniramine controlled-release dosage form

AUTHOR(S): Pao, Li-Heng; Hu, Oliver Yoa-Pu

CORPORATE SOURCE: Sch. Pharmacy, National Defense Medical Center, Taipei, 90048-508, Taiwan

SOURCE: Drug Development and Industrial Pharmacy (1994), 20(17), 2695-706

CODEN: DDIPD8; ISSN: 0363-9045

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A HPLC method that involves the use of a silica gel column and an aqueous mobile phase for simultaneous separation of chlorpheniramine, pseudoephedrine and terfenadine in plasma is presented. Alkalized samples are cleaned by extraction with n-hexane, and the extraction is followed by evaporating the solvent and reconstituting the residue in a small amount of mobile phase. An aliquot of this solution is analyzed by a HPLC system with a silica gel column, an aqueous mobile phase containing 55% MeCN and 45% (NH<sub>4</sub>)H<sub>2</sub>PO<sub>4</sub> (pH 4.0), and UV detection at 210 nm. The low detection limits of the method in plasma are 1 ng, 4 ng and 0.5 ng for chlorpheniramine, pseudoephedrine and terfenadine, resp. In this study, terfenadine acts as an internal standard. The coefficient of variance on the results of intraday and interday precision and the accuracy on control samples of chlorpheniramine and pseudoephedrine were all within 10%. We have used this method successfully in a pilot bioavailability study of a newly developed controlled-release formulation.

L23 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:462347 HCAPLUS

DOCUMENT NUMBER: 119:62347

TITLE: Distribution kinetics of drugs in blood-redistribution phenomenon of thiopentone

AUTHOR(S): Pao, Li Heng; Ho, Shung Tai; Hu, Oliver Yoa Pu

CORPORATE SOURCE: Sch. Pharm., Natl. Def. Med. Cent., Taipei, Taiwan

SOURCE: Zhonghua Yaoxue Zazhi (1993), 45(1), 75-83

CODEN: CYHCEX; ISSN: 1016-1015

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Distribution kinetics of thiopentone in whole blood was studied. After spiking thiopentone (7.5, 15 and 20 µg/mL) to fresh human blood, the redistribution phenomenon of thiopentone from erythrocytes to plasma was observed within at approx. 5 min. The redistribution phenomenon might be attributed to the high lipid-water partition coefficient of natural thiopentone. The mean equilibrium plasma/blood cells ratio and blood cells/plasma distribution coefficient were  $3.44 \pm 0.31$  and  $1.97 \pm 0.32$ , resp., and independent of their initial blood concentration of thiopentone.

The

mean equilibrium plasma/blood cells ratio and blood cells/plasma distribution coefficient were  $3.44 \pm 0.31$  and  $1.97 \pm 0.32$ , resp., and independent of their initial blood concentration of thiopentone. Because the distribution between plasma and blood cells was non instantaneous, the time elapsed between the collection and centrifugation of blood samples may have a significant effect on the measured plasma thiopentone concentration

Distribution

between plasma and blood cells may also occur in a similar manner with other drugs which have a different mechanism of forming a reversible Schiff base on the surface of blood cells membrane. It is recommended that plasma should be separated as soon as the blood sample is collected to obtain an authentic plasma concentration of drugs.

L23 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:91553 HCAPLUS

DOCUMENT NUMBER: 116:91553

TITLE: Determination of fenoverine, a modulator of smooth muscle motility, in capsules and in human plasma: application to dosage form stability and a pilot study in humans

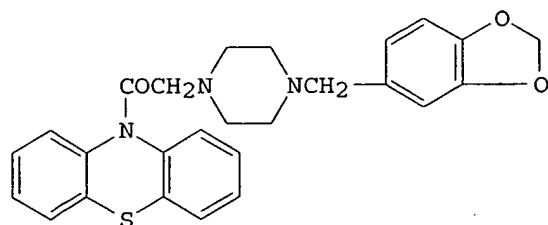
AUTHOR(S): Hu, Oliver Yoa Pu; Chen, Pu Hsiang; Fang, Yaw Ju; Tang, Hung Shang; Pao, Li Heng; Kwok, Kin Man; King, Ming Lu

CORPORATE SOURCE: Sch. Pharm., Natl. Def. Med. Cent., Taipei, Taiwan  
SOURCE: Journal of Pharmaceutical Sciences (1992), 81(1), 91-3  
CODEN: JPMSAE; ISSN: 0022-3549

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Fenoverine (I) is a novel, potent, musculotropic, spasmolytic agent that affects primarily the gastrointestinal tract, bile duct, and female genital organs. A simple, specific, and accurate HPLC method was developed for the determination of I in capsules and plasma. This method has been

successfully applied to stability studies of fenoverine capsules and to a pilot study in a normal, healthy volunteer following oral administration of I. For the determination of I in capsules, a Nucleosil 5- $\mu$ m CN column, with

acetonitrile-0.1 M ammonium acetate (60:40) as mobile phase and detection at 254 nm, was employed. The mean correlation coefficient of the calibration curve ( $n = 6$ ) for the assay was 0.9999 over a concentration range of 24.6-147.6  $\mu$ g/mL I standard solns. I did not decompose significantly at 4, 45, 55, and 65° for 3 mo. The mean correlation coeffs. of within-day and between-day calibration curves were 0.9995 and 0.9999, resp., over a range of 10 to 1000 ng/mL of fenoverine in plasma. The limit of detection was 10 ng in plasma.

Spivack 10\_080043- - Inventor Search

L23 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:11135 HCAPLUS

DOCUMENT NUMBER: 116:11135

TITLE: Pharmacokinetics, pharmacodynamics and relative bioavailability of propranolol tablet in Chinese  
AUTHOR(S): Hu, Oliver Yoa; Chen, Kun Bing; Pao, Li Heng; Kwok, Kin Man; Ho, Shung Tai; Chan, Shu Fei; Lai, Jin Shing; Chung, Ping Hong

CORPORATE SOURCE: Sch. Pharm., Natl. Def. Med. Cent., Taipei, Taiwan

SOURCE: Zhonghua Yaoxue Zazhi (1991), 43(5), 413-23

CODEN: CYHCEX; ISSN: 1016-1015

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two propranolol tablet formulations (Inderal and Cardolol) were bioequivalent in the Chinese populations. Possible differences in propranolol pharmacokinetics and pharmacodynamics among race and living circumstances were observed

L23 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:610474 HCAPLUS

DOCUMENT NUMBER: 111:210474

TITLE: Mechanism of action of 1,2,4-triazolo[1,5-a]pyrimidine sulfonamide herbicides

AUTHOR(S): Subramanian, M. V.; Loney, V.; Pao, L.

CORPORATE SOURCE: Dow Chem. Co., Walnut Creek, CA, 94518, USA

SOURCE: BCPC Monograph (1989), 42(Prospects Amino Acid Biosynth. Inhib. Crop Prot. Pharm. Chem.), 97-100

CODEN: MBCCDO; ISSN: 0306-3941

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 11 refs. indicating that acetolactate synthase is the primary target site for the herbicides sulfometuron, imazethapyr and triazolopyrimidine.

L23 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:641932 HCAPLUS

DOCUMENT NUMBER: 109:241932

TITLE: Built-in space charge at junctions between heavily doped and semiinsulating gallium arsenide layers

AUTHOR(S): Lehovc, K.; Pao, H.

CORPORATE SOURCE: Dep. Electr. Eng., Univ. South. California, Los Angeles, CA, 90089, USA

SOURCE: Solid-State Electronics (1988), 31(9), 1433-40

CODEN: SSELA5; ISSN: 0038-1101

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The thermal equilibrium distributions of carriers, space-charge d. and elec. field in semiinsulating GaAs adjacent to heavily doped GaAs was analyzed in detail and analytic approxns. to these distributions were described. The semiinsulating GaAs is assumed to contain deep donors of the EL2 type and a much smaller concentration of shallow acceptors. The extension of the neg.

built-in space charge layers adjacent to an n+ contact is of the order of the Debye length based on the acceptor concentration rather than on the free-electron concentration. The main portion of the pos. space-charge layer adjacent to a p+ contact is independent of the EL2 and acceptor concns. with the space-charge d. decreasing inversely with the square of the distance from the contact.

L23 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:431565 HCAPLUS  
DOCUMENT NUMBER: 109:31565  
TITLE: Lack of effect of physostigmine on thiopentone plasma protein binding  
AUTHOR(S): Ho, Shung Tai; Pao, Li Heng; Hu, Oliver Yoa Pu  
CORPORATE SOURCE: 1st Dep. Anesthesiol., Natl. Def. Med. Cent., Taipei, Taiwan  
SOURCE: Taiwan Yaoxue Zazhi (1987), 39(3), 135-40  
CODEN: JTPHAO; ISSN: 0368-4520  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The effect of physostigmine on thiopentone plasma protein binding was studied by using dialysis with correction for volume shift. The percent unbound of 10 µg/mL thiopentone with and without 20 ng/mL physostigmine were determined with a pH = 7.4 isotonic buffer solution at 37°. The fraction unbound was calculated using both traditional method and a new equation to allow for volume shift and drug loss during dialysis. The result showed that there was no significant influence of physostigmine on thiopentone plasma protein binding. Therefore, the significantly decreased thiopentone anesthetic effect after physostigmine treatment is not due to the change of thiopentone plasma protein binding.

=>

=> d his ful -120

(FILE 'HOME' ENTERED AT 11:34:11 ON 25 AUG 2006)

FILE 'REGISTRY' ENTERED AT 11:35:22 ON 25 AUG 2006

L1 1 SEA ABB=ON PLU=ON SWERTIAMARIN/CN  
D STAT QUE L1  
D IDE CAN L1 1  
L2 10 SEA ABB=ON PLU=ON (SWERTIAMACR/BI OR SWERTIAMACROSIDE/BI OR  
SWERTIAMAR/BI OR SWERTIAMARIN/BI OR SWERTIAMARINE/BI OR  
SWERTIAMAROSIDE/BI) NOT L1

FILE 'HCAPLUS' ENTERED AT 11:37:06 ON 25 AUG 2006

L3 213 SEA ABB=ON PLU=ON L1 OR ?SWERTIAMARIN?  
L4 48 SEA ABB=ON PLU=ON L3 (L) (?MEDIC? OR ?THERAP? OR ?PHARM? OR  
?DRUG?)  
D STAT QUE  
D IBIB ABS HITSTR L4 1-48

FILE 'REGISTRY' ENTERED AT 11:51:58 ON 25 AUG 2006

L5 1 SEA ABB=ON PLU=ON CYTOCHROME P450/BI

FILE 'HCAPLUS' ENTERED AT 11:54:05 ON 25 AUG 2006

FILE 'REGISTRY' ENTERED AT 11:54:27 ON 25 AUG 2006

L7 SET SMARTSELECT ON  
SEL PLU=ON L5 1- CHEM : 3 TERMS  
SET SMARTSELECT OFF

FILE 'HCAPLUS' ENTERED AT 11:54:27 ON 25 AUG 2006

L8 1 SEA ABB=ON PLU=ON L7  
L9 51451 SEA ABB=ON PLU=ON L8 OR CYTOCHROME (2A) 450 OR CYP3A  
L10 4 SEA ABB=ON PLU=ON L3 AND L9  
L11 1 SEA ABB=ON PLU=ON L10 NOT L4  
D STAT QUE L11  
D IBIB ABS HITSTR L11 1

FILE 'REGISTRY' ENTERED AT 11:57:47 ON 25 AUG 2006

L12 SET SMARTSELECT ON  
SEL PLU=ON L2 1- CHEM : 20 TERMS  
SET SMARTSELECT OFF

FILE 'HCAPLUS' ENTERED AT 11:57:49 ON 25 AUG 2006

L13 28 SEA ABB=ON PLU=ON L12  
L14 202 SEA ABB=ON PLU=ON L13 OR ?SWERTIAM?  
L18 14 SEA ABB=ON PLU=ON (L3 OR L14) (L) INHIBIT?  
L19 5 SEA ABB=ON PLU=ON L18 NOT (L4 OR L11)  
D STAT QUE L19  
D IBIB ABS HITSTR L19 1-5

FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 24 AUG 2006 HIGHEST RN 904307-87-5

DICTIONARY FILE UPDATES: 24 AUG 2006 HIGHEST RN 904307-87-5

Spivack 10\_080043 - - History

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCAPLUS

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 25 Aug 2006 VOL 145 ISS 10  
FILE LAST UPDATED: 24 Aug 2006 (20060824/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

=> fil reg

FILE 'REGISTRY' ENTERED AT 11:35:22 ON 25 AUG 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 24 AUG 2006 HIGHEST RN 904307-87-5  
DICTIONARY FILE UPDATES: 24 AUG 2006 HIGHEST RN 904307-87-5

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

=>

=> d stat que l1

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON SWERTIAMARIN/CN

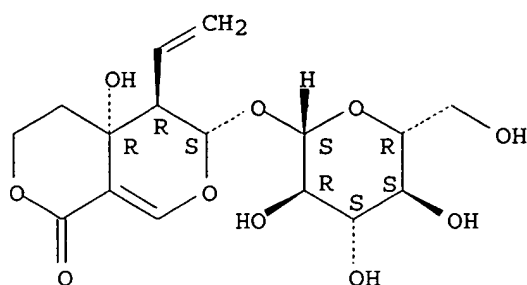
=>

=>

=> d ide can l1 1

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 17388-39-5 REGISTRY  
ED Entered STN: 16 Nov 1984  
CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-  
4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-  
4,4a,5,6-tetrahydro-4a-hydroxy-, [4aR-(4a $\alpha$ ,5 $\beta$ ,6 $\alpha$ )]-  
CN Swertiamarin (6CI, 7CI, 8CI)  
OTHER NAMES:  
CN Swertiamarine  
CN Swertiamaroside  
FS STEREOSEARCH  
DR 28633-33-2  
MF C16 H22 O10  
CI COM  
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAOLD,  
CAPLUS, CHEMCATS, CHEMLIST, CSChem, DDFU, DRUGU, EMBASE, IPA, MEDLINE,  
MRCK\*, NAPRALERT, RTECS\*, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

193 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
193 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
9 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE	1:	145:180622
REFERENCE	2:	145:159735
REFERENCE	3:	144:495524
REFERENCE	4:	144:456392
REFERENCE	5:	144:439546
REFERENCE	6:	144:324786
REFERENCE	7:	144:299597
REFERENCE	8:	144:299321
REFERENCE	9:	144:270581
REFERENCE	10:	144:239871

```
=> => fil hcaplus
```

FILE 'HCAPLUS' ENTERED AT 11:37:06 ON 25 AUG 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.



FILE COVERS 1907 - 25 Aug 2006 VOL 145 ISS 10  
FILE LAST UPDATED: 24 Aug 2006 (20060824/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> => d stat que

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON SWERTIAMARIN/CN  
L3 213 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR ?SWERTIAMARIN?  
L4 48 SEA FILE=HCAPLUS ABB=ON PLU=ON L3(L) (?MEDIC? OR ?THERAP? OR  
?PHARM? OR ?DRUG?)

=> d ibib abs hitstr l4 1-48

L4 ANSWER 1 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2006:585215 HCAPLUS  
TITLE: Seven constituents in nine species of Tibetan medicine  
"Zangyinchen"  
AUTHOR(S): Yang, Huiling; Liu, Jianquan  
CORPORATE SOURCE: Northwest Institute of Plateau Biology, Chinese  
Academy of Sciences, Xining, Qinghai Province, 810001,  
Peop. Rep. China  
SOURCE: Zhongcaoyao (2005), 36(8), 1233-1237  
CODEN: CTYAD8; ISSN: 0253-2670  
PUBLISHER: Zhongcaoyao Zazhi Bianjibu  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese  
AB Effective chemical constituents in nine species of Tibetan medicine  
"Zangyinchen" including Swertia mussoti, Swertia franchetiana, Swertia  
przewalskii, Swertia erythrosticta, Swertia tetraptera, Swertia  
macrosperma, Lomatogonium carinthiacum, Swertia chirayiata and Halenia  
elliptica were studied, and the medicinal values of these plants  
were confirmed based on differences in their chemical constituents and  
physiol. activities. Contents of 7 constituents, swertiamarin,  
mangiferin, swertisin, oleanolic acid, 1,5,8-trihydroxy-3-methoxyxanthone,  
1,8-dihydroxy-3,7-dimethoxyxanthone and 1,8-dihydroxy-3,5-  
dimethoxyxanthone, were detected by high performance liquid chromatog.  
(HPLC). There were significant differences in the contents of effective  
constituents among the nine species. Different species of Swertia should  
be selected to prepare Tibetan medicine "Zangyinchen" according to  
the functions of different chemical constituents.

L4 ANSWER 2 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2006:519583 HCAPLUS  
DOCUMENT NUMBER: 145:159735  
TITLE: Effects of gentiopicroside, sweroside and  
swertiamarine, secoiridoids from gentian (Gentiana  
lutea ssp. symphyandra), on cultured chicken embryonic  
fibroblasts  
AUTHOR(S): Ozturk, Nilgun; Korkmaz, Seval; Ozturk, Yusuf; Baser,  
K. Husnu Can  
CORPORATE SOURCE: Faculty of Pharmacy, Department of Pharmacognosy,  
Anadolu University, Eskisehir, Turk.  
SOURCE: Planta Medica (2006), 72(4), 289-294  
CODEN: PLMEAA; ISSN: 0032-0943  
PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Wound healing properties of Gentian (*Gentiana lutea* ssp. *symphyandra*) extract and its main constituents, gentiopicroside, sweroside and swertiamarine (compds. 1-3, resp.) were evaluated by comparison with dexpanthenol on cultured chicken embryonic fibroblasts. The extract was also analyzed by HPLC to quantify its constituents. Chicken embryonic fibroblasts from fertilized eggs were incubated with the plant extract and its constituents, compds. 1-3. Using microscopy, mitotic ability, morphol. changes and collagen production in the cultured fibroblasts were evaluated as parameters. Wound healing activity of Gentian seems to be mainly due to the increase in the stimulation of collagen production and the mitotic activity by compds. 2 and 3, resp. ( $p < 0.005$  in all cases). All three compds. also exhibited cytoprotective effects, which may cause a synergism in terms of wound healing activity of Gentian. The findings demonstrated the wound healing activity of Gentian, which has previously been based only on ethnomedical data.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:301740 HCAPLUS  
DOCUMENT NUMBER: 144:324786  
TITLE: Cytochrome P450 2C9 inhibitors  
INVENTOR(S): Hu, Oliver Yoa-Pu; Wang, Hong-Jaan; Hsiong, Cheng-Huei; Pao, Li-Heng  
PATENT ASSIGNEE(S): Taiwan  
SOURCE: U.S. Pat. Appl. Publ., 15 pp.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006069042	A1	20060330	US 2004-948206	20040924
PRIORITY APPLN. INFO.:			US 2004-948206	20040924

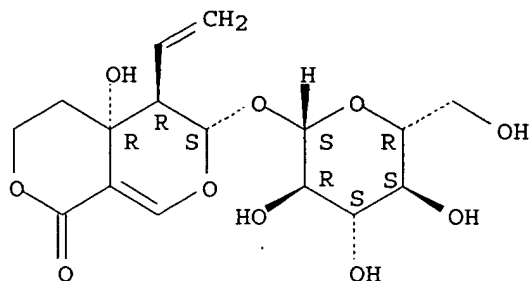
AB This invention is to provide multiple specific inhibitors of cytochrome P 450 isoenzyme CYP2C9. These inhibitors can be derived from any combinations with the following compds. including: Tamarixetin, Formononetin, isoliquiritigenin, Phloretin, luteolin, Quercitrin, quercetin, myricetin, Wongonin, Puerarin, Genistein, Nordihydroguaiaretic acid, Narigenin, Capillarisin, Chrysin, Fisetin, eriodictyol, 6-Gingerol, Isorhamnetin, isoquercitrin, Morin, (+)-Taxifolin, isovitexin, 3-Phenylpropyl Acetate, Oleanolic acid, ursolic acid,  $\beta$ -Myrcene, cinnamic acid, Luteolin-7-Glucoside, Liquiritin, (+)Limonene, Homoorientin, Swertiamarin, Embelin, Daidzein, Poncirin, (-)-Epicatechin, ergosterol. These natural products can be used to enhance the bioavailability of therapeutic agents (drugs).

IT 17388-39-5, Swertiamarin  
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cytochrome P 450 2C9 inhibitors for enhancing drug bioavailability)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:235889 HCAPLUS

DOCUMENT NUMBER: 145:180622

TITLE: Gastroprotective effects of bitter principles isolated from Gentian root and Swertia herb on experimentally-induced gastric lesions in rats

AUTHOR(S): Niiho, Yujiro; Yamazaki, Takashi; Nakajima, Yoshihiro; Yamamoto, Toshinori; Ando, Hidehiro; Hirai, Yasuaki; Toriizuka, Kazuo; Ida, Yoshiteru

CORPORATE SOURCE: Tsukuba Research Institute, Ohta's Isan Co, Ltd., 957 Shishiko, Ushiku, Ibaraki, 300-1231, Japan

SOURCE: Journal of Natural Medicines (2006), 60(1), 82-88

CODEN: JNMOBN

PUBLISHER: Springer Tokyo

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Gentianae Radix, the dried root and rhizoma of *Gentiana lutea* L. (Gentianaceae), has long been used as a remedy for liver and stomach inflammation, eye troubles, etc. In this paper, the gastroprotective effects of the methanol extract of Gentian root (GM) were studied using different gastric lesion models. In pylorus-ligated rats, administration of GM in the duodenum suppressed gastric juice secretion and total acid output in a dose-dependent manner. Oral or duodenum administration of GM showed significant protection against acute gastric ulcer induced by aspirin plus pylorus ligation, water-immersion restraint stress-induced ulcers, and gastric mucosal injury induced by ethanol. Furthermore, four secoiridoid glycosides, amarogentin (A1), gentiopicroside (A2), amaroswerin (A3), and swertiamarin (A4), were obtained from Gentian root or Swertia herb, and their protective effects against stress-induced ulcers and ethanol-induced gastric mucosal injury were evaluated. The doses required for 50% inhibition (ID50) of A1, A3, and A4 on stress-induced ulcers were calculated to be 5.76, 2.58, and 167 mg/kg resp. The protective effect of A2 at 250 mg/kg was 26.5%. On ethanol-induced gastritis, 5.0 mg/kg of A1 and A3 showed remarkable suppressive effects (33.7 and 45.4%, resp.), and 20 mg/kg of A4 exhibited a suppressive effect (30.8%). The effects of A1, A3, and A4 on ethanol-induced gastric lesions were canceled by 5.0 mg/kg indomethacin pretreatment. These results suggest that the therapeutic effects of Gentian root on gastric lesions are associated with enhanced mucosal defensive factors via the prostaglandin pathway in the cell membrane, and that secoiridoid glycosides contribute to this activity.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:164629 HCAPLUS  
 DOCUMENT NUMBER: 144:239871  
 TITLE: Inhibitors and enhancers of uridine  
 diphosphate-glucuronosyltransferase 2b (ugt2b)  
 INVENTOR(S): Oliver, Yoa-Pu Hu; Hsiong, Cheng-Huei; Wang, Mei-Ting;  
 Pao, Li-Heng  
 PATENT ASSIGNEE(S): National Defense Medical Center, Taiwan; National  
 Defense University  
 SOURCE: U.S. Pat. Appl. Publ., 27 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006040875	A1	20060223	US 2005-28615	20050105
WO 2006072203	A1	20060713	WO 2005-CN2167	20051213
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: TW 2004-93100465 A 20040128  
 US 2005-28615 A 20050105

AB A UGT2B inhibitor capable of increasing the bioavailability of a drug, being a compound in a free base or a pharmaceutically acceptable salt form that is selected from the group consisting of: capillarisin, isorhamnetin,  $\beta$ -naphthoflavone,  $\alpha$ -naphthoflavone, hesperetin, terpineol, (+)-limonene,  $\beta$ -myrcene, swertiamarin, eriodictyol, cineole, apigenin, baicalin, ursolic acid, isovitexin, lauryl alc., puerarin, trans-cinnamaldehyde, 3-phenylpropyl acetate, isoliquiritigenin, paeoniflorin, gallic acid, genistein, glycyrrhizin, protocatechuic acid, Et myristate, umbelliferone, and a combination thereof. A UGT2B enhancer capable of enhancing the liver detoxification function in a subject, being a compound in a free base or a pharmaceutically acceptable salt form that is selected from the group consisting of: mordihydroguaiaretic acid, wogonin, trans-cinnamic acid, baicalein, quercetin, daidzein, oleanolic acid, homoorientin, hesperetin, narigin, neohesperidin, (+) epicatechin, hesperidin, liquiritin, eriodictyol, formononetin, quercitrin, genkwanin, kaempferol, isoquercitrin, (+)-catechin, naringenin, daidzin, (-)epicatechin, luteolin-7-glucoside, ergosterol, rutin, luteolin, Et myristate, apigenin, 3-phenylpropyl acetate, umbelliferone, glycyrrhizin, protocatechuic acid, poncirin, isovitexin, 6-gingerol, cineole, genistein, trans-cinnamaldehyde, and a combination thereof. Rat were administered with both 100 mg/Kg nalbuphine and 4 mg/Kg capillarisin orally. The T<sub>max</sub> and C<sub>max</sub> for nalurphin was 25 min, and 2582 ng/mL resp., as compared with 97 min and 79 ng/mL for the control group which did not receive capillarsisin.

ACCESSION NUMBER: 2006:47597 HCAPLUS  
 DOCUMENT NUMBER: 144:299321  
 TITLE: Swertiamarin injection and its preparation and use  
 INVENTOR(S): Zhou, Chunxiang  
 PATENT ASSIGNEE(S): Kunming Tongchi Pharmaceutical Research and  
 Development Co., Ltd., Peop. Rep. China  
 SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.  
 CODEN: CNXXEV  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Chinese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1634099	A	20050706	CN 2003-10121024	20031231
PRIORITY APPLN. INFO.:			CN 2003-10121024	20031231

AB The title injection(injection solution or powder) is composed of dry >90% swertiamarin 50-100 and pharmaceutic accessory 0-50%. The pharmaceutic accessory contains solubilizer and/or skeleton supporting agent, antioxidant. The solubilizer and/or skeleton supporting agent is mannitol, lactose, glucose, dextraven, polyethylene pyrrolidone, glycine and/or urea. The antioxidant is vitamin C, Na<sub>2</sub>SO<sub>3</sub>, NaHSO<sub>3</sub>, sodium pyrosulfate and/or sodium thiosulfate. The swertiamarin injection is prepared by extracting swertiamarin from Gentianaceae, Scrophulariaceae or Oleaceae, mixing with accessory and injection water at 30-60 ° for 10-20 min, cooling, filtering with microporous filter membrane, superfilter membrane, standing filter solution at 0-5 ° for 1-48 h, further filtering, canning, freeze drying, sterilizing and packaging. The swertiamarin injection is used for preparing drug for preventing and treating live-gallbladder disease, virus hepatitis or drug-injured hepatitis, cholecystitis or gastrointestinal tract spasm.

L4 ANSWER 7 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1228163 HCAPLUS  
 DOCUMENT NUMBER: 144:103961  
 TITLE: Isolation of iridoid and secoiridoid glycosides and comparative study on Radix gentianae and related adulterants by HPLC analysis  
 AUTHOR(S): Jiang, Ren-Wang; Wong, Ka-Lok; Chan, Yiu-Man; Xu, Hong-Xi; But, Paul Pui-Hay; Shaw, Pang-Chui  
 CORPORATE SOURCE: Institute of Chinese Medicine, Shatin, The Chinese University of Hong Kong, New Territories, Hong Kong, Peop. Rep. China  
 SOURCE: Phytochemistry (Elsevier) (2005), 66(22), 2674-2680  
 CODEN: PYTCAS; ISSN: 0031-9422  
 PUBLISHER: Elsevier Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB HPLC profile guided study led to the isolation of an acylated secoiridoid glycoside, named gentiotrifloroside (1), together with six known compds., i.e., loganic acid (2), 6-O-β-D-glucopyranosylgentiopicroside (3), swertiamarin (4), gentiopicroside (5), sweroside (6) and 2-(o,m-dihydroxybenzoyl)-sweroside (7) from Gentiana triflora and Gentiana rigescens. The structure of 1 was deduced from one- and two-dimensional NMR spectroscopic expts. Compds. 1-7 were used successfully as chemical markers for the comparison of the four species of Gentiana used as Radix gentianae. Addnl., differentiation of Gentiana species mentioned and those used as adulterants was evaluated. The close similarity of chemical

composition among the four genuine *Gentiana* species explain their popular usage as *R. gentianae* in Chinese medicine. We have also shown that the variation of chemical composition in *R. gentianae* and related adulterants agree well with their botanical phylogeny.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1199899 HCAPLUS

DOCUMENT NUMBER: 144:299597

TITLE: *Swertia chirata* Buch.-Ham. ex Wall. (Gentianaceae), an endangered Himalayan medicinal plant: comparative study of the secondary compound patterns in market drug, in vitro-cultivated, and micropropagated field grown samples

AUTHOR(S): Wawrosch, Christoph; Hugh-Bloch, Andreas; Hostettmann, Kurt; Kopp, Brigitte

CORPORATE SOURCE: Department of Pharmacognosy, University of Vienna, Vienna, A-1090, Austria

SOURCE: *Scientia Pharmaceutica* (2005), 73(3), 127-137  
CODEN: SCPHA4; ISSN: 0036-8709

PUBLISHER: Oesterreichische Apotheker-Verlagsgesellschaft

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Samples of the Himalayan medicinal plant *Swertia chirata* obtained from a local market in Nepal, from a micropropagated field cultivated clone, and from two in vitro-clones were compared by means of HPLC. The substance patterns of methanolic and dichloromethane exts. of the in vivo grown materials showed good conformity while in the samples from tissue culture major compds. were missing. Our findings confirm that the secondary metabolism of in vitro-cultivated plants normally differs from that of plants in their natural environment. Furthermore, the compound pattern of plants produced through micropropagation and subsequently cultivated in the field is comparable to that of plants collected from the wild. As an alternative to the uncontrolled depletion of the natural resources a sustainable use of *Swertia chirata* could hence be achieved by controlled field culture of micropropagated plants.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1180733 HCAPLUS

DOCUMENT NUMBER: 144:495524

TITLE: Dynamic accumulation determination of six medicinal bioactive components in *Swertia mussotii* Franch. during different growth period

AUTHOR(S): Ma, Yuhua; Ji, Lanju; Ji, Wenhe; Chen, Guichen; Lu, Xuefeng

CORPORATE SOURCE: Northwest Plateau Institute of Biology, Chinese Academy of Sciences, Xining, 810001, Peop. Rep. China

SOURCE: *Xibei Zhiwu Xuebao* (2005), 25(2), 393-396  
CODEN: XZXUEV; ISSN: 1000-4025

PUBLISHER: Kexue Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The contents of six medicinal bioactive components in *Swertia mussotii* Franch. during different growth periods were determined by reversed-phase high performance liquid chromatog. The anal. was performed on Kromasil Cve (250 mm t4.6 mm, 5 i.m.) eluted with methanol and 0.02% aqueous phosphoric acid as mobile phase and UV detection at 260 nm. The good linear relationships

and recoveries were obtained under the optimum conditions for every component. The results showed that the whole plant should be harvest during Sept. and Oct.

IT 17388-39-5, Swertiamarin

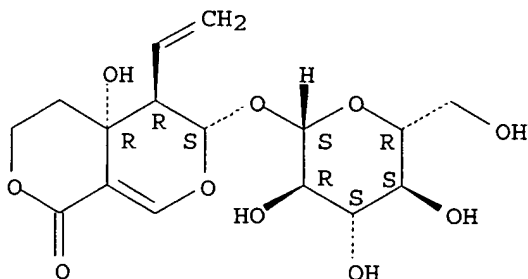
RL: ANT (Analyte); ANST (Analytical study)

(determination of medicinal components of *Swertia mussoitii* by reversed-phase HPLC)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 10 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:759940 HCAPLUS

DOCUMENT NUMBER: 144:11236

TITLE: Glycoside constituents from *Swertia franchetiana*

AUTHOR(S): Wang, Shisheng; Xu, Qing; Xiao, Hongbin; Liu, Xiumei; Du, Yuguang; Han, Xiuwen; Liang, Xinmiao

CORPORATE SOURCE: Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, Liaoning Province, 116011, Peop. Rep. China

SOURCE: Zhongcaoyao (2004), 35(8), 847-849

CODEN: CTYAD8; ISSN: 0253-2670

PUBLISHER: Zhongcaoyao Zazhi Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Glycosides from a Tibetan medicine, *Swertia franchetiana* H.

Smith, were isolated and studied. The constituents were isolated and purified by column chromatog. methods. Their structures were identified on the basis of physiochem. properties and spectral anal. Eleven compds. were obtained from the aqueous parts of the methanol extract and identified as mangiferin (I), isoorientin (II), swertisin (III), swertianolin (IV), 1-O-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranosyl]-3,5-dimethoxy-xanthone (V), 1-O- $\beta$ -D-glucopyranosyl-3,7,8-trimethoxyxanthone (VI), 1-O-[ $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 6)- $\beta$ -D-glucopyranosyl]-2,3,5-trimethoxyxanthone (VII), and 1-oxoisochroman-5-carboxaldehyde (VIII), swertiamarin (IX), gentipicroside (X), sweroside (XI). Compds. VI-XI were first found from this plant, and VII was obtained from the plants of *Swertia* L. for the first time.

L4 ANSWER 11 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

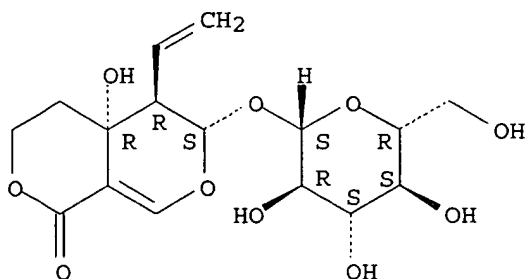
ACCESSION NUMBER: 2005:219144 HCAPLUS

DOCUMENT NUMBER: 143:312166

TITLE: Variation of active constituents of an important Tibet folk medicine *Swertia mussoitii* Franch. (Gentianaceae) between artificially cultivated and naturally

distributed  
 AUTHOR(S): Yang, Huiling; Ding, Chenxu; Duan, Yuanwen; Liu, Jianquan  
 CORPORATE SOURCE: Qinghai-Tibet Plateau Biological Evolution and Adaptation Laboratory, Northwest Plateau Institute of Biology, Chinese Academy of Sciences, Qinghai, 810001, Peop. Rep. China  
 SOURCE: Journal of Ethnopharmacology (2005), 98(1-2), 31-35  
 CODEN: JOETD7; ISSN: 0378-8741  
 PUBLISHER: Elsevier Ireland Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Concns. of 7 phytochem. constituents (swertiamarin, mangiferin, swertisin, oleanolic acid, 1,5,8-trihydroxy-3-methoxyxanthone, 1,8-dihydroxy-3,7-dimethoxyxanthone, and 1,8-dihydroxy-3,5-dimethoxyxanthone) of "ZangYinChen" (*Swertia mussotii*, a herb used in Tibetan folk medicine) were determined and compared in plants collected from naturally distributed high-altitude populations and counterparts that had been artificially cultivated at low altitudes. Levels of mangiferin, the most abundant active compound in this herb, were significantly lower in cultivated samples and showed a neg. correlation with altitude. The other constituents were neither pos. nor neg. correlated with cultivation at low altitude. Concns. of all of the constituents varied substantially with growth stage and were highest at the bud stage in the cultivars, but there were no distinct differences between flowering and fruiting stages in this respect.  
 IT 17388-39-5, Swertiamarin  
 RL: ANT (Analyte); ANST (Analytical study)  
 (variation of active constituents between artificially cultivated and naturally distributed *Swertia mussotii* used in Tibet folk medicine)  
 RN 17388-39-5 HCAPLUS  
 CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:1068867 HCAPLUS  
 DOCUMENT NUMBER: 143:189384  
 TITLE: Development of monoclonal antibody against isoquinoline alkaloid coptisine and its application for the screening of medicinal plants  
 AUTHOR(S): Kim, Jun-Sik; Tanaka, Hiroyuki; Yuan, Chun-Su; Shoyama, Yukihiro



CORPORATE SOURCE: Department of Pharmacognosy, Graduate School of  
Pharmaceutical Sciences, Kyushu University, 3-1-1  
Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan  
SOURCE: Cytotechnology (2004), 44(3), 115-123  
CODEN: CYTOER; ISSN: 0920-9069  
PUBLISHER: Kluwer Academic Publishers  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In the development of immunoassay technique, the design of hapten containing a functional group suitable for protein conjugate is the key step for the preparation of antibodies against small mols. Coptisine (MW 320), a bioactive constituent of Berberis and Coptis species, is small as an immunogen. In addition, coptisine has no reactive group in mol. for conjugating with a protein. To overcome this problem, 9-O-carboxymethyl-berberrubine was designed and conjugated with carrier protein. In order to confirm its immunogenicity, the ratio of hapten in the conjugate was determined by matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF MS). After immunization, hybridomas secreting antibodies against coptisine were produced by fusing splenocytes with mouse myeloma cell line, P3-X63-Ag8-653. Among hybridomas, the clone 2A1 secreting anti-coptisine monoclonal antibody (MAb) 2A1-9E-1 was obtained through the limited dilution method. The MAb-based ELISA against coptisine was developed and characterized. The linear range of the assay in this ELISA method was extended from 1.56 to 25 µg ml<sup>-1</sup> possessing the detection limit of 1.56 µg ml<sup>-1</sup>. The established ELISA using MAb 2A1-9E-1 was applied for the survey of isoquinoline alkaloids in various medicinal plants.

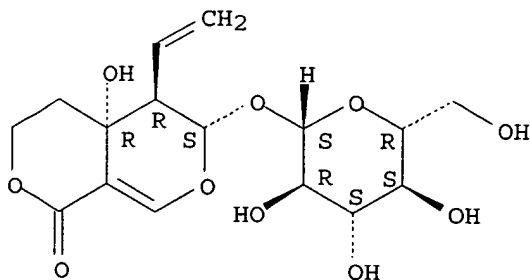
IT 17388-39-5, Swertiamarin

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(no MAb 2A1-9E-1 cross-reactivity with; development of monoclonal antibody against isoquinoline alkaloid coptisine and its application for screening of medicinal plants)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-(β-D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1067334 HCAPLUS

DOCUMENT NUMBER: 142:151296

TITLE: Liquid culture system for shoot multiplication and secoiridoid production in micropropagated plants of Centaurium erythraea Rafn

AUTHOR(S): Piatczak, Ewelina; Wielanek, Marzena; Wysokinska, Halina  
 CORPORATE SOURCE: Department of Biology and Pharmaceutical Botany, Medical University, Lodz, 91 151, Pol.  
 SOURCE: Plant Science (Amsterdam, Netherlands) (2005), 168(2), 431-437  
 CODEN: PLSCE4; ISSN: 0168-9452  
 PUBLISHER: Elsevier B.V.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB An efficient shoot multiplication method from shoot tips of *Centaurium erythraea* using liquid Murashige and Skoog (MS) medium supplemented with indole-3-acetic acid (IAA) (0.1 mg l<sup>-1</sup>) and 6-benzylaminopurine (BAP) (1.0 mg l<sup>-1</sup>) was developed. Under these conditions, almost 60 microshoots per explant were produced within 4 wk. This is three times more as compared to shoots obtained on agar-solidified medium. Shoots taken from liquid culture were rooted with frequency 85% and 77% on hormone-free full-strength and half-strength MS medium, resp. within 6 and 4 wk. The plantlets were transferred into soil and they survived acclimatization with 90% success, producing healthy plants, morphol. similar to plants derived from shoots grown on solid culture during their multiplication stage. The shoots of 10-wk-old micropropagated plants of *C. erythraea* accumulated secoiridoid glucosides (gentiopicricoside, swertiamarin and sweroside) up to 149 mg g<sup>-1</sup> dry weight. The value was significantly higher than those achieved for other tested plant materials, such as shoot cultures and aerial parts of wild-grown plants. It is hoped, that the system using liquid shoot culture could be useful for large-scale micropropagation of *C. erythraea* plants with high production of pharmacol. important products.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:919504 HCAPLUS  
 DOCUMENT NUMBER: 142:162598  
 TITLE: Agent for inhibiting/promoting activities of cytochrome p450 1A (cyp1a)  
 INVENTOR(S): Hu, You-pu; Wang, Jau-r; Shiung, Jeng-huei  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: Taiwan, 4 pp.  
 CODEN: TWXXA5  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Chinese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
TW 581687	B	20040401	TW 2000-89116955	20000821
PRIORITY APPLN. INFO.:			TW 2000-89116955	20000821

AB The present invention discloses ingredients capable of inhibiting or enhancing the activities of Cytochrome P 450 1A (CYP1A), in which 44 compds., e.g. Kaempferol, Luteolin-7-Glycoside, Terpineol, Alpha-Naphthoflavone, Hesperetin, etc. have inhibitory effects; and 43 compds., e.g. (-)-Epicatechin, Cineole, Narigin, Protocatechuic acid, etc. have enhancing effects. However, the inhibiting or enhancing effects are related to the concentration thereof. The CYP1A inhibitors can reduce the first pass metabolism generated in a clin. medicine so that the dosage of the medicine will not be reduced and the medicinal effect can be increased, as

well as providing new ways of making medicine.

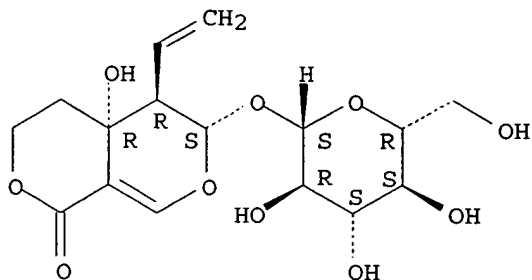
IT 17388-39-5, Swertiamarin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compns. containing inhibitors or agonists of  
cytochrome P 450 1A)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-  
4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:768956 HCAPLUS

DOCUMENT NUMBER: 141:301576

TITLE: Quantitative determination of swertiamarin in Swertia  
davidi Franch. by HPLC

AUTHOR(S): Xu, Xiuying; Tang, Chunhong; Zheng, Yimin; Fu,  
Shanquan

CORPORATE SOURCE: Chongqing Academy of Chinese Materia Medica,  
Chongqing, 400065, Peop. Rep. China

SOURCE: Zhongguo Yaoke Daxue Xuebao (2003), 34(5), 475-476  
CODEN: ZHYXE9; ISSN: 1000-5048

PUBLISHER: Zhongguo Yaoke Daxue

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The content of swertiamarin in Swertia davidi Franch. was determined by HPLC at  
254 nm on Phenomenex luna C18 column with methanol-water (20:80) as mobile  
phase and flow rate of 0.8 mL/min. The linear range was 0.37-2.775 mg/mL  
( $r = 0.9997$ ). The average recovery was 99.74% with RSD of 1.58%. The method  
was simple and easy to determine the content of swertiamarin in Swertia davidi  
Franch.

L4 ANSWER 16 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:136067 HCAPLUS

DOCUMENT NUMBER: 140:169813

TITLE: Separation and determination of gentiopicroside and  
swertiamarin in Tibetan medicines by  
micellar electrokinetic electrophoresis

AUTHOR(S): Zhao, Shengguo; Liu, Qing; Chen, Xingguo; Hu, Zhide

CORPORATE SOURCE: College of Chemistry and Chemical Engineering, Lanzhou  
University, Lanzhou, 730000, Peop. Rep. China

SOURCE: Biomedical Chromatography (2004), 18(1), 10-15  
CODEN: BICHE2; ISSN: 0269-3879

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Micellar electrokinetic electrophoresis was employed to determine 2 active

components, gentiopicroside (GE) and swertiamarin (SW) in one Tibetan preparation medicine named shiweilongdankeli, 2 Tibetan herbal medicines named *Gentiana rhodantha* and *G. kitag* and 3 other Chinese *Gentiana* medicines named *G. scabra*, *G. regescens* and *G. macrophylla*. The dissociation consts. of gentiopicroside and swertiamarin determined by MEKC were 7.71 and 6.25. The optimum buffer system was 70 mM borate-10 mM sodium dodecylsulfate (SDS) -6% (volume/volume) isopropanol (pH 9.0). The voltage was 15 kV and detection was at 254 nm. The lower limits of detection (defined as a signal-to-noise ratio of about 3) were approx. 3.86 mg L<sup>-1</sup> for GE and 5.88 mg L<sup>-1</sup> for SW. The relative standard deviation of the migration time and peak area of the GE and SW were 2.33, 2.47 and 1.27, 2.19%, resp. and the recoveries of the 2 compds. were 96-104% for GE and 92-102% for SW.

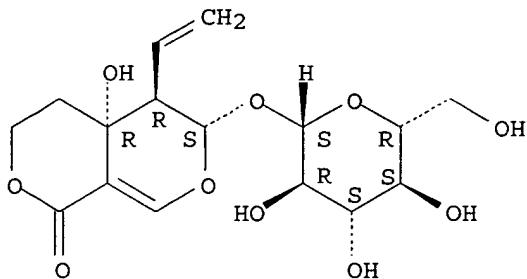
IT 17388-39-5, Swertiamarin

RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)  
(separation and determination of gentiopicroside and swertiamarin in Tibetan medicines by MEKC)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:861857 HCAPLUS

DOCUMENT NUMBER: 140:344642

TITLE: Development of a method to reduce microbial numbers in powdered crude drugs by a copper-alcohol treatment

AUTHOR(S): Sakagami, Yoshikazu; Yamasaki, Katsuhiko

CORPORATE SOURCE: Osaka Prefectural Institute of Public Health, Osaka, 537-0025, Japan

SOURCE: Biocontrol Science (2003), 8(3), 119-122

CODEN: BISCFY; ISSN: 1342-4815

PUBLISHER: Society for Antibacterial and Antifungal Agents, Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effectiveness of a copper-alc. treatment to reduce the microbial nos. in the powdered crude drugs was investigated. Furthermore, the effect on the chemical quality control was also evaluated. After the treatment, no microorganisms and no changes in the appearance of the crude drugs were found. Furthermore, no remarkable change in the contents of index components in the powdered crude drugs was found except for that of swertiamarin and gentiopicroside in gentian and that of ginsenoside Rb1 and Rg1 in ginseng. These results suggest that this treatment method would be very useful to reduce the number of

microorganisms in powdered crude drugs.

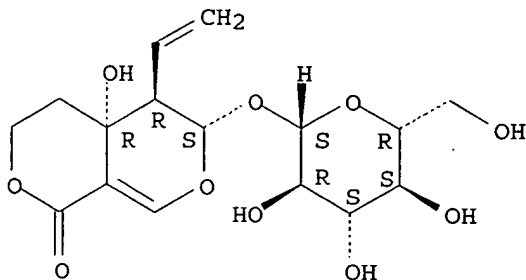
IT 17388-39-5, Swertiamarin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(reduction of microbial nos. in powdered crude drugs by copper-alc.  
treatment)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-  
4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:696527 HCAPLUS

DOCUMENT NUMBER: 139:207741

TITLE: Cytochrome p450 3A inhibitors and enhancers

INVENTOR(S): Hu, Oliver Yoa-pu; Hsiong, Cheng-huei; Kuo, Benjamin  
Pei-chung; Pao, Li-heng

PATENT ASSIGNEE(S): Taiwan

SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003166584	A1	20030904	US 2002-80043	20020222
PRIORITY APPLN. INFO.:			US 2002-80043	20020222

AB The present invention provides cytochrome P 450 3A (CYP3A) inhibitors and enhancers. Examples of the CYP3A inhibitors include free bases or pharmacol. acceptable salts of at least one of the following compds.:  $\alpha$ - and  $\beta$ -naphthoflavone, apigenin, baicalein,  $\beta$ -myrcene, catechin, 3-phenylpropyl acetate, formononetin, gallic acid, hesperetin, hesperidin, isoquercitrin, lauryl alc., luteolin, luteolin 7-glycoside, narigin, nordihydroguaiaretic acid, quercitrin, swertiamarin, terpineol, and trans-cinnamaldehyde. Examples of the CYP3A enhancers include free bases or pharmacol. acceptable salts of at least one of the following compds.: apigenin, formononetin, and luteolin-7-glycoside. The CYP3A inhibitors can be used, alone or co-administered with a drug, to improve the drug bioavailability. The CYP3A inhibitors can also be used as chemopreventors to prevent biotransformation of procarcinogenic compds. into carcinogens via CYP3A activity or for treatment of intestinal or hepatic cancer by inhibit the CYP3A activity. The CYP3A enhancers can be used to improve

the enzymic activity of CYP3A so as to improve the biotransformation and degradation of active drugs or the substrates of CYP3A from the body. The CYP3A inhibitors and enhancers of the present invention are natural substances extracted from herbs and non-toxic.

L4 ANSWER 19 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:543321 HCAPLUS

DOCUMENT NUMBER: 139:358078

TITLE: Bioactivity of secoiridoid glycosides from *Centaureum erythraea*

AUTHOR(S): Kumarasamy, Y.; Nahar, L.; Cox, P. J.; Jaspars, M.; Sarker, S. D.

CORPORATE SOURCE: Phytopharmaceutical Research Laboratory, School of Pharmacy, The Robert Gordon University, Aberdeen, UK

SOURCE: Phytomedicine (2003), 10(4), 344-347

CODEN: PYTOEY; ISSN: 0944-7113

PUBLISHER: Urban & Fischer Verlag GmbH & Co. KG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As part of our on-going search for bioactive compds. from Scottish plants, two secoiridoid glycosides, swertiamarin and sweroside, have been isolated from the aerial parts of *Centaureum erythraea* Rafn (Family: Gentianaceae) by reversed-phase preparative HPLC coupled with a photo-diode-array detector. The structures of these compds. were elucidated unambiguously by UV, FABMS and extensive 1D and 2D NMR spectroscopic analyses and also by comparing exptl. data with literature data. Antibacterial, free radical scavenging activities and general toxicity of these glycosides have been assessed. Both compds. inhibited the growth of *Bacillus cereus*, *Bacillus subtilis*, *Citrobacter freundii* and *Escherichia coli*. While swertiamarin was also active against *Proteus mirabilis* and *Serratia marcescens*, sweroside inhibited the growth of *Staphylococcus epidermidis*. Swertiamarin and sweroside exhibited significant general toxicity in brine shrimp lethality bioassay and the LD50 values were 8.0 µg/mL and 34 µg/mL, resp., whereas that of the pos. control podophyllotoxin, a well known cytotoxic lignan, was 2.79 µg/mL. Chemotaxonomic implications of these compds. in the family Gentianaceae have also been discussed briefly.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:3766 HCAPLUS

DOCUMENT NUMBER: 136:366375

TITLE: Studies on the efficacious chemical constituents of medicinal of *Swertia davidi*

AUTHOR(S): Peng, Xiaochun; Wang, Huixian; Chen, Shiguo; Zhou, Saiqin

CORPORATE SOURCE: College of Life Science and Chemistry, Jishou University, Jishou, 416000, Peop. Rep. China

SOURCE: Jishou Daxue Xuebao, Ziran Kexueban (2001), 22(3), 59-60

CODEN: JDXXFY; ISSN: 1007-2985

PUBLISHER: Jishou Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Five efficacious chemical constituents were isolated from *S. davidi*. Three of them were identified as swertiamarin, ursolic acid, and oleanolic acid by chemical and spectral analyses. The total flavonol content of *S. davidi* was determined by HPLC, and its amount was 1.54%.

IT 17388-39-5P, Swertiamarin

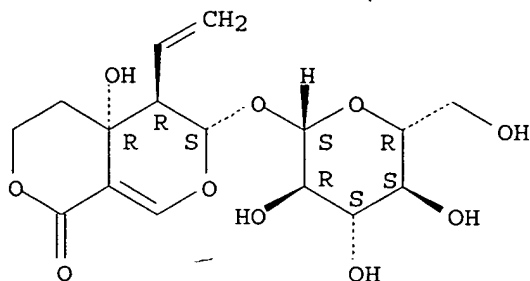
RL: PUR (Purification or recovery); PREP (Preparation)

(efficacious chemical constituents of medicinal of Swertia  
davidi)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-  
4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 21 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:630566 HCAPLUS

DOCUMENT NUMBER: 136:319321

TITLE: Liver-protective activities of aucubin derived from  
traditional oriental medicine

AUTHOR(S): Chang, Il-Moo

CORPORATE SOURCE: Natural Products Research Institute and Graduate  
Studies in Natural Products Science, Seoul National  
University, Seoul, 150-747, S. Korea

SOURCE: Emerging Drugs (Westbury, NY, United States) (2001),  
1(Molecular Aspects of Asian Medicines), 109-124  
CODEN: EDWNA

PUBLISHER: DJP Publications Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The iridoid glycosides including aucubin (AU), catalpol (CA),  
swertiamarin (SW), and gardenoside (GA) are frequently found as  
natural constituents of many traditional oriental medicinal  
plants including Chinese herbs. Among these iridoid glycosides, AU was  
systematically studied for its potent liver-protective activities using  
exptl. systems of hepatic damage. AU showed high liver-protective  
activity against carbon tetrachloride-induced hepatic damage in mice.  
Also AU showed significant protective activity against  
 $\alpha$ -amanitin-induced hepatic damage in mice, and it prevented a  
depression of liver RNA biosynthesis caused by  $\alpha$ -amanitin  
administration. Potent antidotal effects on mushroom poisoning in beagle  
dogs ingested with aqueous extract of *Amanita virosa* was observed; beagle dogs  
completely survived, even when AU administration was withheld for half an  
hour after mushroom poisoning. In addition, AU was found to suppress  
hepatitis B viral DNA replication in vitro. Conversion of AU to its  
aglycon form appeared to be a prerequisite step for an exhibition of such  
antiviral activity.

IT 17388-39-5, Swertiamarin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

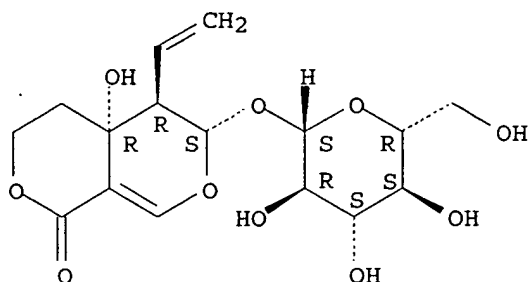
(hepatoprotective action of aucubin derived from traditional oriental  
medicine)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-

4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:557001 HCAPLUS

DOCUMENT NUMBER: 135:170566

TITLE: Analysis of swertiamarin in Swertia herb and preparations containing this crude drug by capillary electrophoresis

AUTHOR(S): Takei, Harumi; Nakauchi, Kimie; Yoshizaki, Fumihiko

CORPORATE SOURCE: Tohoku Pharmaceutical University, Sendai, 981-8558, Japan

SOURCE: Analytical Sciences (2001), 17(7), 885-888

CODEN: ANSCEN; ISSN: 0910-6340

PUBLISHER: Japan Society for Analytical Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Capillary electrophoresis was used to sep. and determine the quantity of swertiamarin in Swertia herb. Subsequently, the authors applied the same anal. condition to estimate the swertiamarin contents in Japanese Pharmacopoeia stomachic prepns., in OTC gastroenteric drugs and in OTC hair tonics containing Swertia herb.

IT 17388-39-5P, Swertiamarin

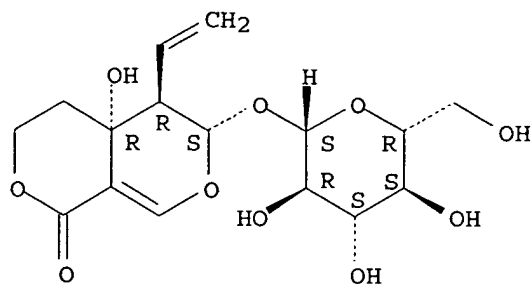
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses) (anal. of swertiamarin in Swertia herb and prepns. containing crude drug by capillary electrophoresis)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:233348 HCAPLUS

DOCUMENT NUMBER: 135:362426

TITLE: Factors affecting the establishment of *Gentiana davidii* var. *Formosana* (Hayata) T. N. Ho cell suspension cultures

AUTHOR(S): Chueh, Fu-Shin; Chen, Chung-Chuan; Tsay, Hsin-Sheng  
CORPORATE SOURCE: Institute of Chinese Pharmaceutical Science, China Medical College, Taichung, 40421, Taiwan

SOURCE: Yaowu Shipin Fenxi (2000), 8(4), 297-303

CODEN: YSFEEP; ISSN: 1021-9498

PUBLISHER: National Laboratories of Food and Drugs, Dep. of Health, Executive Yuan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *Gentiana davidii* var. *Formosana* (Hayata) T. N. Ho (Gentianaceae), commonly known as long-dan in Chinese, is a perennial herb indigenous to Taiwan. It is distributed throughout the island, ranging from low to high elevations. The roots, which contain bitter-tasting secoiridoid glucosides, are used in traditional Chinese medicine. It is mainly used in the treatment of gastrointestinal tract diseases. Continuous collection of plant material from natural habitat has led to the depletion of *Gentiana* population. The purpose of this study was to establish the cell suspension cultures of *Gentiana*, which could be used for large-scale production of active principles such as gentiopicroside and swertiamarin. Callus was initiated by culturing stem explants of *G. davidii* var. *Formosana* on Murashige and Skoog's (1962) basal medium supplemented with 0.2 mg/L 6-furfurylaminopurine (kinetin) and 1.0 mg/L  $\alpha$ -naphthaleneacetic acid (NAA). Fast-growing suspension cell cultures were established by subculturing the callus in MS basal medium (pH 4.2-5.2) supplemented with 0.2 mg/L kinetin and 3% sucrose. The cultures were incubated on an orbital shaker (80-100 rev/min) at  $25 \pm 1$  and low light intensity ( $2.33 \mu\text{E} \cdot \text{m}^{-2} \cdot \text{s}^{-1}$ ).

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:176334 HCAPLUS

DOCUMENT NUMBER: 135:24757

TITLE: Quantitative determination of secoiridoid glucosides in in vitro propagated plants of *Gentiana davidii* var. *formosana* by high performance liquid chromatography

AUTHOR(S): Chueh, Fu-Shin; Chen, Chung-Chuan; Sagare, Abhay P.; Tsay, Hsin-Sheng

CORPORATE SOURCE: Institute of Chinese Pharmaceutical Science, China  
Medical College, Taichung, Taiwan  
SOURCE: Planta Medica (2001), 67(1), 70-73  
CODEN: PLMEAA; ISSN: 0032-0943  
PUBLISHER: Georg Thieme Verlag  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A simple protocol for in vitro mass propagation of *Gentiana davidii* var. *formosana* (Gentianaceae) has been developed. Multiple shoot development was achieved by culturing the stem node explants on Murashige and Skoog (MS) medium supplemented with 4.44  $\mu$ M N6-benzyladenine (BA). The shoots were multiplied by subculturing on MS medium supplemented with 1.07 - 10.74  $\mu$ M  $\alpha$ -naphthaleneacetic acid (NAA) and 8.88  $\mu$ M BA. Shoots were rooted on MS basal medium supplemented with various auxins. Shoots rooted on growth regulator-free medium were transferred to peat moss:vermiculite mixture and acclimatized in the growth chamber. The contents of gentiopicoside and swertiamarin, the two important secoiridoid glucosides, in different plant material were determined by high performance liquid chromatog. (HPLC). The anal. revealed that the content of gentiopicoside and swertiamarin in the aerial and underground parts of *G. davidii* var. *formosana* was higher than the marketed crude drug (underground parts of *G. scabra*) and varied with the age of the plant.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:139579 HCAPLUS  
DOCUMENT NUMBER: 132:185508  
TITLE: Determination of swertiamarin in complex Yugan capsules by HPLC  
AUTHOR(S): Chen, Jiachun; Hu, Junlin  
CORPORATE SOURCE: Hubei Institute of Traditional Chinese Medicine, Wuhan, 430061, Peop. Rep. China  
SOURCE: Yaowu Fenxi Zazhi (2000), 20(1), 51-52  
CODEN: YFZADL; ISSN: 0254-1793  
PUBLISHER: Yaowu Fenxi Zazhi Bianji Weiyuanhui  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

AB The complex Yugan capsule preparation was made from several traditional Chinese medicines, and *Swertia punicea*, was the main component, and swertiamarin was the main compound. The content of swertiamarin in complex Yugan capsules was determined by HPLC on a Spherisorb C18 column with MeOH-H<sub>2</sub>O as the mobile phase and detection at 235 nm. The linearity was between 0.53-2.63  $\mu$ g with  $r = 0.9999$ . The mean recovery was 99.6% with RSD 2.2%. The sample solution was stable, and its RSD was 1.0% within 24 h.

L4 ANSWER 26 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:149699 HCAPLUS  
DOCUMENT NUMBER: 130:320805  
TITLE: Liver-protective activities of aucubin derived from traditional oriental medicine  
AUTHOR(S): Chang, Il-Moo  
CORPORATE SOURCE: Natural Products Research Institute and Graduate Studies in Natural Products Science, Seoul National University, Seoul, 150-460, S. Korea  
SOURCE: Research Communications in Molecular Pathology and Pharmacology (1998), 102(2), 189-204  
CODEN: RCMPE6; ISSN: 1078-0297

PUBLISHER: PJD Publications Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

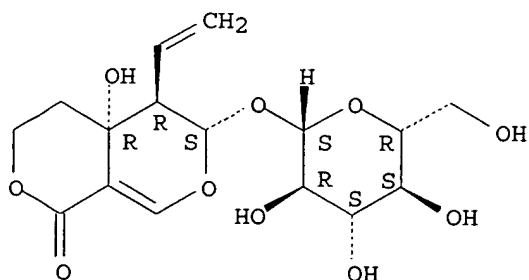
AB The iridoid glycosides including aucubin (AU), catalpol (CA), swertiamarin (SW), and gardenoside (GA) are frequently found as natural constituents of many traditional oriental medicinal plants including Chinese herbs. Among these iridoid glycosides, AU was systematically studied for its potent liver-protective activities using exptl. systems of hepatic damage. AU showed high liver-protective activity against carbon tetrachloride-induced hepatic damage in mice. Also AU showed significant protective activity against  $\alpha$ -amanitin-induced hepatic damage in mice, and it prevented a depression of liver RNA biosynthesis caused by  $\alpha$ -amanitin administration. Potent antidotal effects on mushroom poisoning in beagle dogs ingested with aqueous extract of *Amanita virosa* was observed; beagle dogs completely survived, even when AU administration was withheld for half an hour after mushroom poisoning. In addition, AU was found to suppress hepatitis B viral DNA replication in vitro. Conversion of AU to its aglycon form appeared to be a prerequisite step for an exhibition of such antiviral activity.

IT 17388-39-5, Swertiamarin  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (liver-protective activities of aucubin and other iridoid glycosides derived from traditional oriental medicine)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:799852 HCAPLUS

DOCUMENT NUMBER: 130:71523

TITLE: Pyranopyranone compound-containing HS P47 formation inhibitors for therapeutic use

INVENTOR(S): Morino, Masayoshi; Tsuzuki, Tomoko; Shirakami, Toshimi; Kiyosuke, Yoichi; Yoshikumi, Chikao

PATENT ASSIGNEE(S): Kureha Chemical Industry Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10330268	A2	19981215	JP 1997-151557	19970526

PRIORITY APPLN. INFO.: JP 1997-151557 19970526

OTHER SOURCE(S): MARPAT 130:71523

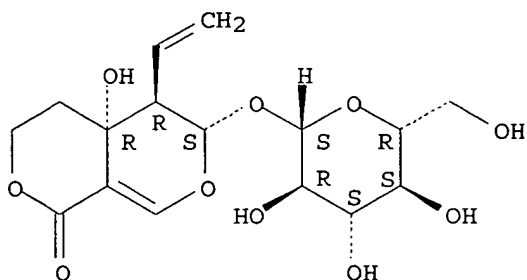
AB HS P47 formation inhibitors containing pyranopyranone compound [markush given; such as Swertiamarin] extracted from Swertia for treatment of chronic renal insufficient, cirrhosis, lung disease and heart hypertrophy are claimed. The compound also can incorporated into health food.

IT 17388-39-5P, Swertiamarin  
 RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (pyranopyranone compound-containing HS P47 formation inhibitors for therapeutic use)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 28 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:267458 HCAPLUS

DOCUMENT NUMBER: 124:325125

TITLE: Enicostema littorale: a new source of swertiamarin

AUTHOR(S): Anwar, Munir; Ahmad, Mansoor; Aslam, Muhammad; Aftab, Khalid

CORPORATE SOURCE: Eli-lilly Scientific Office Pakistan, Karachi, Pak.

SOURCE: Pakistan Journal of Pharmaceutical Sciences (1996), 9(1), 29-35  
 CODEN: PJPSEN; ISSN: 1011-601X

PUBLISHER: University of Karachi, Faculty of Pharmacy

DOCUMENT TYPE: Journal

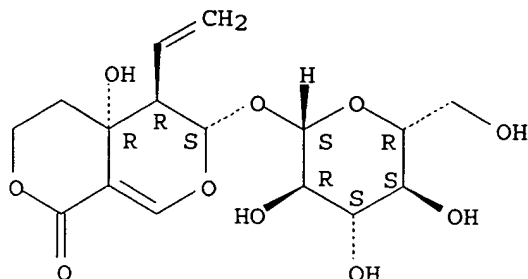
LANGUAGE: English

AB Enicostema littorale, a useful medicinal herb, was subjected to phytochem. as well as pharmacol. investigations. A secoiridoid glycoside, swertiamarin, was isolated and identified on the basis of UV, IR, mass and NMR spectroscopic measurements. However, pharmacol. studies on the blood pressure of rats and ileum of guinea-pig could not provide significant results.

IT 17388-39-5P, Swertiamarin  
 RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)  
 (phytochem. and pharmacol. study on swertiamarin from Enicostema littorale)

RN 17388-39-5 HCAPLUS  
 CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-  
 4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 29 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:821315 HCAPLUS  
 DOCUMENT NUMBER: 123:251301  
 TITLE: Xanthenes and flavonoids of *Lomatogonium rotatum*  
 AUTHOR(S): Khishgee, D.; Pureb, O.  
 CORPORATE SOURCE: Inst. Nar. Med., Ulan-Bator, Mongolia  
 SOURCE: Khimiya Prirodnkh Soedinenii (1993), (5), 761-2  
 CODEN: KPSUAR; ISSN: 0023-1150

PUBLISHER: Fan  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian

AB Chromatog. anal. of the shoots of *Lomatogonium rotatum* (Gentianaceae), a plant used in Tibetan folk-medicine, revealed the presence of 1-hydroxy-3,7,8-trimethoxyxanthone, 1,8-dihydroxy-3,5-dimethoxyxanthone, luteolin, 6-C- $\beta$ -D-glucopyranosylluteolin, and swertiamarin.

L4 ANSWER 30 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1995:288931 HCAPLUS  
 DOCUMENT NUMBER: 122:64531  
 TITLE: HPLC determination of swertiamarin in *Swertia punicea* Hemsl  
 AUTHOR(S): Chen, Jiachun; Chen, Gaiping; Qiao, Ming; Hu, Junlin  
 CORPORATE SOURCE: Hubei Coll. Traditional Chin. Medicine, Wuhan, 430060, Peop. Rep. China  
 SOURCE: Zhongguo Yiyuan Yaoxue Zazhi (1994), 14(8), 356-8  
 CODEN: ZYYAEP; ISSN: 1001-5213  
 PUBLISHER: Zhongguo Yiyuan Yaoxue Zazhi Bianji Weiyuanhui  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese

AB The determination of swertiamarin in *swertia punicea* hemsl by RP-HPLC is reported. The chromatog. consisted of schimadzu LC-5A pump, SPD-2A UV-detector, a schimadzu R-112 data processor and a spherisorb C18 5  $\mu$ m column. Thus, 0.25 g of the powdered drug was accurately weighed and mixed with 20 mL of methanol and refluxed for 40 min in an ultrasonic generator. Methanol was added up to 25 mL, then filtered; 5  $\mu$ L of the filtrate was injected and eluted with methanol-water (1:4) at a low rate of 0.8 mL/min. The peaks were detected at 254 nm, the content was calculated automatically by the data processor.

L4 ANSWER 31 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1992:476479 HCAPLUS

DOCUMENT NUMBER: 117:76479  
 TITLE: Composition comprising plant components for AIDS treatment  
 INVENTOR(S): Tilgner, Regina  
 PATENT ASSIGNEE(S): Germany  
 SOURCE: Ger. Offen., 2 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4120296	A1	19920319	DE 1991-4120296	19910628
PRIORITY APPLN. INFO.:			DE 1991-4120296	19910628

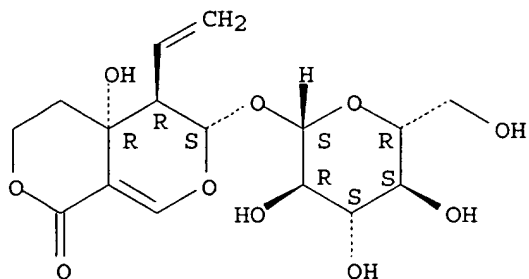
AB A composition for the treatment of AIDS comprises tannins, essential oils, m-cresol, sesquiterpenes, flavonols, glycerides, sugars, vitamin C, estrogens, cations, anions, etc. (no data).

IT 17388-39-5, Swertiamarin  
 RL: BIOL (Biological study)  
 (AIDS treatment by drug containing)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 32 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:91527 HCAPLUS

DOCUMENT NUMBER: 116:91527

TITLE: Simultaneous determination of five bitter secoiridoid glycosides in nine Chinese Gentiana species used as the Chinese drug "Long Dan" by high-performance liquid chromatography

AUTHOR(S): Zhang, J. S.; Tian, Z. X.; Lou, Z. C.

CORPORATE SOURCE: Sch. Pharm., Beijing Med. Univ., Beijing, 100083, Peop. Rep. China

SOURCE: Yaoxue Xuebao (1991), 26(11), 864-70  
 CODEN: YHHPAL; ISSN: 0513-4870

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB A new and rapid HPLC method for the simultaneous determination of five bitter secoiridoid glycosides (gentiopicroside, swertiamarin, sweroside, amarogentin, and amaroswerin) in the Chinese drug Long dan roots of *G. manshurica*, and 8 other species has been developed. A column and MeOH-H<sub>2</sub>O as the mobile phase were used. The bitter

secoiridoid glycosides were detected at 254 nm and the anal. was successfully carried out within 23 min. This method is sensitive, accurate and has good reproducibility. Recoveries of each secoiridoid glycoside were 100.0-101.5% with coeffs. of variation 0-2.5%.

L4 ANSWER 33 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:428535 HCAPLUS

DOCUMENT NUMBER: 111:28535

TITLE: Pharmaceuticals containing plant secoiridoids for treatment of gastritis and ulcer

INVENTOR(S): Shinbo, Yujiro; Nakajima, Kajiro; Ishiwatari, Hiroe; Yamazaki, Ritsu; Ito, Hiroshi

PATENT ASSIGNEE(S): Ohta's Isan Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

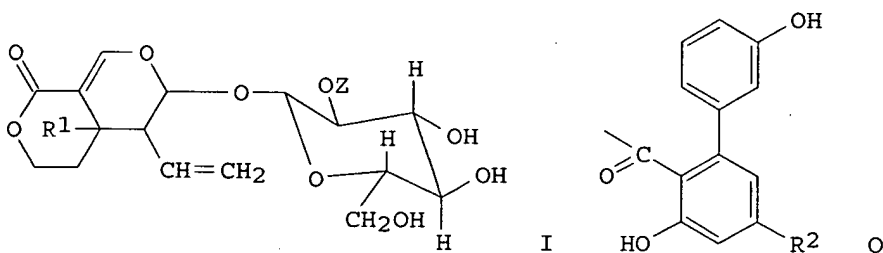
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

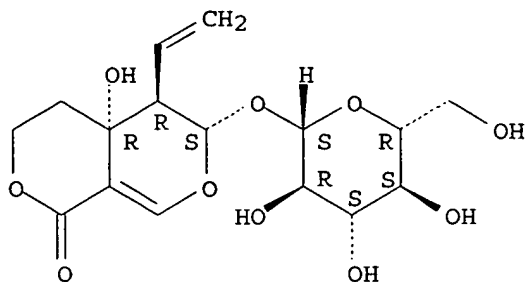
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63190827	A2	19880808	JP 1987-24248	19870203
JP 05035131	B4	19930525		
PRIORITY APPLN. INFO.: GI			JP 1987-24248	19870203



- AB Pharmaceuticals for treatment and prevention of ulcer and gastritis contain secoiridoids, or their glycosides, swertiamarin (I; R1 = OH, Z = H), amarogentin (I; R1 = H, Z = Q, R2 = OH), amaroswerin (I; R1 = OH, Z = Q, R2 = OH), and amaropanin (I; R1 = H, Z = Q, R2 = H). Amarogentin at 5 mg/kg orally given to rats prior to subjecting these animals to physiol. stress by keeping them in water for 7 h, prevented gastric ulcer formation to a greater extent than did Aldioxa, a com. antiulcer drug. Amarogentin 5, lactose 93, crystalline cellulose 20, and Mg stearate 7 g were mixed and made into tablets (125 mg/tablet). Amarogentin (600 mg) was isolated from 250 g Swertia japonica, by using MeOH as the extracting solvent and subjecting the extract to a series of chromatog. column containing Sephadex LH-20 and silica gel.
- IT 17388-39-5, Swertiamarin  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceuticals containing, for gastritis and ulcer treatment)
- RN 17388-39-5 HCAPLUS
- CN 1H,3H-Pyran[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 34 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:485019 HCAPLUS

DOCUMENT NUMBER: 105:85019

TITLE: Separation and identification of gentiopicroside, swertiamarin and sweroside in the traditional drug longdan, Radix Gentianae

AUTHOR(S): Luo, Jipeng; Lou, Zhican

CORPORATE SOURCE: Coll. Pharm., Beijing Med. Univ., Beijing, Peop. Rep. China

SOURCE: Zhongcaoyao (1986), 17(4), 145-9

CODEN: CTYAD8; ISSN: 0253-2670

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The active components of longdan (*Gentiana* roots, especially those from *G. manschurica* and *G. scabra*) were separated by silica gel and polyacrylamide column chromatog., using  $\text{CHCl}_3$ -MeOH- $\text{H}_2\text{O}$  (10:2:1) and EtOAc-MeOH- $\text{H}_2\text{O}$  (100:5:2), resp., as eluting solvent systems. Gentiopicroside (I) [20831-76-9] and swertiamarin (II) [17388-39-5] were separated from the root extract of *G. manschurica*, and sweroside [14215-86-2], I and II were separated from the root extract of *G. scabra*. The mass spectral fragmentation patterns of these 3 components and tetraacetylswertiamarin [10289-37-9] are also given.

L4 ANSWER 35 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:213344 HCAPLUS

DOCUMENT NUMBER: 104:213344

TITLE: TLC-densitometry determination of bitter glycosides in the Chinese drug Longdan, radix *Gentianae*, and its quality evaluation

AUTHOR(S): Luo, Jipeng; Lou, Zhican

CORPORATE SOURCE: Coll. Pharm., Beijing Med. Univ., Beijing, Peop. Rep. China

SOURCE: Yaoxue Xuebao (1986), 21(1), 40-6

CODEN: YHHPAL; ISSN: 0513-4870

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB The plant origin of Longdan, *Gentianae* root, in Chinese market was investigated and 9 species of the genus *Gentiana* were involved. The contents of gentiopicroside [20831-76-9], swertiamarin [17388-39-5] and sweroside [14215-86-2] are used as criteria of quality of the crude drug Longdan. TLC-densitometry was used to determine the glucosides. A linear relation between the amount of glucoside

(<8

$\mu\text{g}$ ) and absorbance was obtained for each bitter glycoside when using the following parameters: dual wavelength (sample wavelength: gentiopicroside 270 nm, swertiamarin 240 nm, sweroside 245 nm;



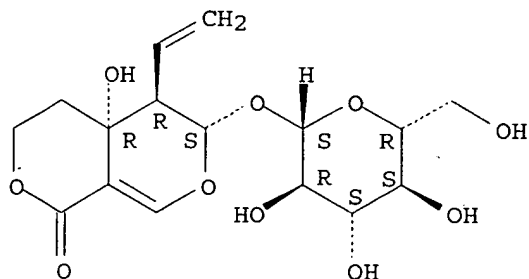
reference wavelength: 400 nm), reflection mode, and linear scanning. Absolute MeOH was better than aqueous MeOH or 95% EtOH for extracting gentiopicroside from the crude drug. The ultrasonic extraction method is superior to the cold or hot maceration method for its simplicity, rapidity and avoiding the interference of heat, especially for heat-sensitive components. Glycosides were well separated by using EtOAc-MeOH-H<sub>2</sub>O (20:2:1) as developing solvent. The spots were determined directly by a dual wavelength TLC-scanner. The average recovery of the 3 bitter glycosides for 3 detns. was 99.23-100.20% with a relative standard deviation 0.8-1.7%. The result of quant. detns. of the 3 bitter glucosides in crude drugs derived from 8 *Gentiana* species showed that the content of gentiopicrosid and total bitter glucosides is higher (4.06-5.82% and 4.35-6.65%, resp.) in drugs derived from *G. rigescens*, *G. triflora*, *G. atuntsiensis*, *G. manshurica* (Heilongjiang) and *G. scabra* (Liaoning) and lower (1.84-3.12% and 2.07-3.12%, resp.) in underground parts of *G. cephalantha* and *G. suffrutescens*. Gentiopicroside contents in the aerial parts of the latter 2 species were so poor (1.06 and 0.2%, resp.) that these aerial parts, especially that of *G. suffrutescens*, are not considered suitable for use as the drug Longdan.

IT 17388-39-5  
 RL: ANT (Analyte); ANST (Analytical study)  
 (determination of, in Gentian root Chinese drug by TLC-densitometry)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-(β-D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 36 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:554067 HCAPLUS

DOCUMENT NUMBER: 103:154067

TITLE: Antihepatotoxic principles of *Swertia japonica* herbs

AUTHOR(S): Hikino, Hiroshi; Kiso, Yoshinobu; Kubota, Masatoshi; Hattori, Masao; Namba, Tsuneo

CORPORATE SOURCE: Pharm. Inst., Tohoku Univ., Sendai, Japan

SOURCE: Shoyakugaku Zasshi (1984), 38(4), 359-60  
 CODEN: SHZAA; ISSN: 0037-4377

DOCUMENT TYPE: Journal

LANGUAGE: English

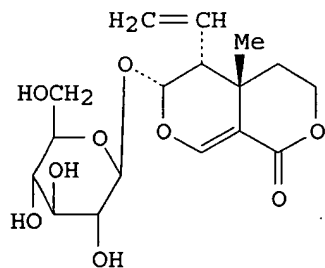
AB Active constituents of the herb *S. japonica* (amarogentin [21018-84-8], amaroswerin [21233-18-1], swertiamarin [17388-39-5], swertiamarin acetate [98668-34-9], homoorientin [4261-42-1], swertiajaponin [6980-25-2], swertisin [6991-10-2], bellidifolin [2798-25-6], methylbellidifolin [521-65-3], methylswertianin [22172-17-4], and oleanolic acid [508-02-1] all appear to contribute to

the prevention of CCl<sub>4</sub>- or galactosamine-induced damage to primary cultured rat hepatocytes by the crude drug senburi.

L4 ANSWER 37 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1985:172481 HCAPLUS  
 DOCUMENT NUMBER: 102:172481  
 TITLE: Silica gel thin layer and polyamide sheet chromatographic identification of the secoiridoid glucosides in certain Gentiana species used in the Chinese traditional medicine Long Dan  
 AUTHOR(S): Luo, Jipeng; Lou, Zhicen  
 CORPORATE SOURCE: Fac. Pharm., Beijing Med. Coll., Beijing, Peop. Rep. China  
 SOURCE: Yaowu Fenxi Zazhi (1985), 5(1), 7-10  
 CODEN: YFZADL; ISSN: 0254-1793  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese

AB Gentiopicroside [20831-76-9], swertiamarin [17388-39-5], sweroside [14215-86-2], amarogentin [21018-84-8] and amaroswerin [21233-18-1] in Gentiana were separated and identified by polyamide sheet chromatog. Silica gel TLC was unable to sep. all 5 glucosides. G. manshurica, G. seabra, G. triflora, G. atuntriensis, G. rigescens, G. cephalantha And G. suffrutescens contained gentiopicroside, swertiamarin, and sweroside. G. triflora, G. atuntriensis And G. rigescens contained amarogentin but none of the medicinal plants contained amaroswerin. The content of gentiopicroside in underground parts was higher than that in aerial parts.

L4 ANSWER 38 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1983:27691 HCAPLUS  
 DOCUMENT NUMBER: 98:27691  
 TITLE: Central depressant effect of swertiamarin  
 AUTHOR(S): Lei, Weiya; Shi, Quantao; Yu, Sichang  
 CORPORATE SOURCE: Yunnan Inst. Pharmacol., Peop. Rep. China  
 SOURCE: Zhongcaoyao (1982), 13(8), 368-9  
 CODEN: CTYAD8; ISSN: 0253-2670  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese  
 GI



I

AB I.p. injected swertiamarin (I) [17388-39-5] (400 mg/kg) produced marked analgesic effect in mice; the analgesic effect of 400 mg I/kg was comparable to that of 10 mg morphine/kg or 20 mg L-tetrahydropalmatine/kg. The analgesic effect of I lasted longer than that of other analgesics tested, but the analgesia-inducing time of I was longer than that of the other analgesics tested. I also markedly

decreased the spontaneous activity in mice, prolonged thiopental sodium-induced sleep in rabbits, induced sedation in pigeons, and was synergistic with Na barbiturate in mice, indicating central depressing effects of I. The analgesic, sedative, and the previously reported antispastic effects of I all indicate the pharmacol. significance of I as an analgesic.

L4 ANSWER 39 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1982:223362 HCAPLUS

DOCUMENT NUMBER: 96:223362

TITLE: Analytical studies on the active components of crude drugs. VI. Determination and stability of swertiamarin in pharmaceutical preparations containing powdered Swertia herb

AUTHOR(S): Tashiro, Yumiko; Mitani, Yoko; Murata, Koji; Yoshida, Akiyoshi; Hayashi, Shin Ich

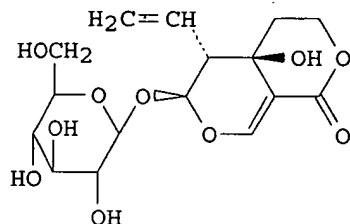
CORPORATE SOURCE: Res. Dev. Dep., Rohto Pharm. Co., Ltd., Osaka, Japan  
SOURCE: Yakugaku Zasshi (1982), 102(3), 258-63

CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

GI



I

AB In a simple and rapid high-performance liquid chromatog. (HPLC) procedure for the determination of swertiamarin (I) [17388-39-5] in pharmaceutical prepns., I is extracted with water, and the extract is purified with a Sep-Pak C18 cartridge before anal. I was separated with a mobile phase of H<sub>2</sub>O-MeCN (9:1) on a Nucleosil 10C18 column. The stability of I in pharmaceutical prepns. was investigated also. The combination of Swertia herb powder with antacids accelerated the decomposition of I, and crude drugs and digestive enzymes did not have any significant effect on stability. The decomposition of I in aqueous solution

was a pseudo first-order reaction.

IT 17388-39-5

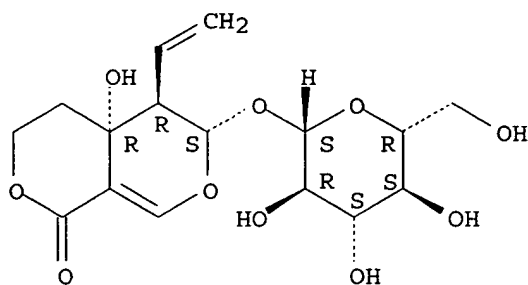
RL: ANT (Analyte); ANST (Analytical study)

(determination of, in pharmaceuticals by high-performance liquid chromatog., stability in relation to)

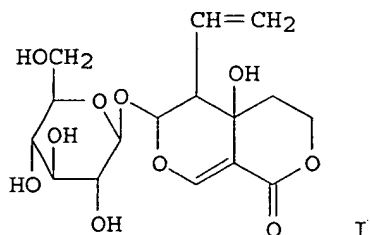
RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-(β-D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



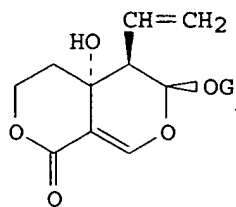
L4 ANSWER 40 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1980:645549 HCAPLUS  
 DOCUMENT NUMBER: 93:245549  
 TITLE: High-speed liquid chromatographic analysis of  
 drugs. XI. Quantitative determination of  
 Swertiamarin in Swertiae Herba  
 AUTHOR(S): Akada, Yoshinobu; Kawano, Sadako; Tanase, Yaichiro  
 CORPORATE SOURCE: Fac. Pharm. Sci., Tokushima Univ. Arts Sci.,  
 Tokushima, Japan  
 SOURCE: Yakugaku Zasshi (1980), 100(7), 770-3  
 CODEN: YKKZAJ; ISSN: 0031-6903  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese  
 GI



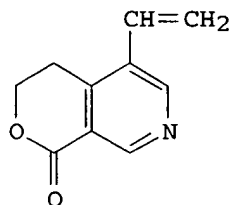
AB Swertiamarin (I) [17388-39-5], the bitter component of the herb of *Swertia japonica*, was determined by high-speed liquid chromatog. I in *Swertia Herba* was separated on a 20 cm column of LiChrosorb RP-8, using the Shimadzu Du Pont LC-3A liquid chromatog. with 1.5% THF as the desorption solution. Detection was achieved at 235 nm. The precision of this method was .apprx.±1% and the detection limit was several ng. I in *Swertia Herba* was extracted with water and the extract was injected directly into the column. The content of I was calculated from the calibration curve of the previously prepared standard. The cycle time of anal. was .apprx.15 min. This method is considered to be useful for the evaluation of *Swertia Herba*.

L4 ANSWER 41 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1979:115084 HCAPLUS  
 DOCUMENT NUMBER: 90:115084  
 TITLE: Biologically active principles of crude drugs  
 : pharmacological actions of *Swertia japonica* extracts, swertiamarin and gentianine

AUTHOR(S): Yamahara, Johji; Konoshima, Takao; Sawada, Tokunosuke;  
 Fujimura, Hajime  
 CORPORATE SOURCE: Kyoto Coll. Pharm., Kyoto, Japan  
 SOURCE: Yakugaku Zasshi (1978), 98(11), 1446-51  
 CODEN: YKKZAJ; ISSN: 0031-6903  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese  
 GI



I, G=?-D-glucopyranosyl



II

AB The pharmacol. effect of a methanolic extract of *S. japonica*, swertiamarin (I) [17388-39-5] being the main secoiridoid glucoside of this herb and gentianine (II) [439-89-4] obtained from swertiamarin in aqueous ammonia, were investigated in mice and rats. II depressed the central nervous system, had antiulcerogenic actions, and inhibited gastric secretion, whereas the other had no appreciable action.

IT 17388-39-5

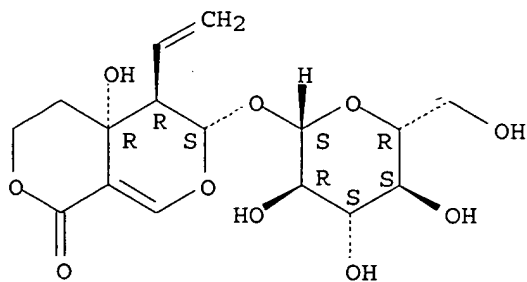
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmacol. of)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-(β-D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



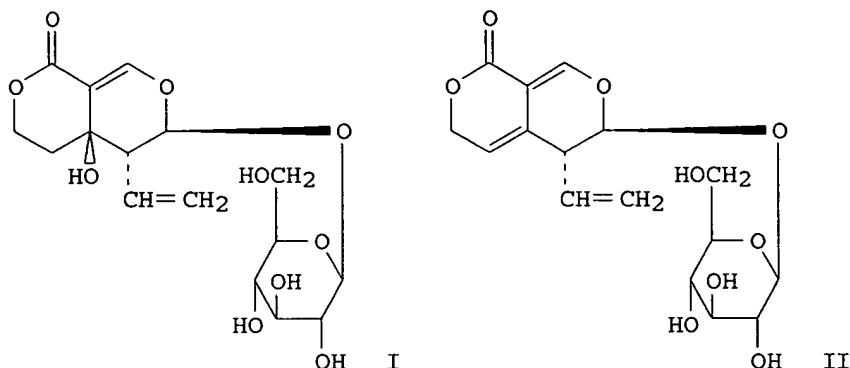
L4 ANSWER 42 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1978:568999 HCAPLUS

DOCUMENT NUMBER: 89:168999

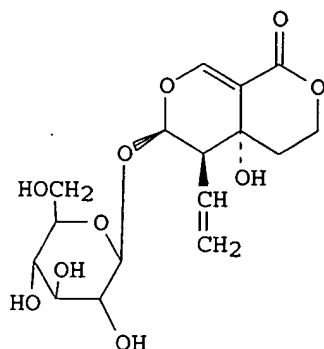
TITLE: Studies on crude drugs from *Gentiana scabra*.  
 5. Determination of *Gentianae Radix* and *Swertiae Herba* dispensed in bitter peptic preparations in J.P. VIII and stability of bitter principles  
 gentiopicroside and swertiamarin

AUTHOR(S): Hayashi, Teruaki; Kosiro, Chuichi  
 CORPORATE SOURCE: Res. Lab., Koshirochuji Shoten Co. Ltd., Osaka, Japan  
 SOURCE: Yakuzaigaku (1976), 36(2), 95-100  
 CODEN: YAKUA2; ISSN: 0372-7629  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Japanese  
 GI



AB To determine the presence of Gentianae Radix and Swertiae Herba dispensed in the bitter peptic preps. in Japanese Pharmacopeia VIII, a simple and effective method was developed, by which other cheaper bitter crude drugs are readily detected. Since both Gentianae Radix and Swertiae Herba are often dispensed with NaHCO<sub>3</sub> stability of their major bitter principles, gentiopicroside (I) [20831-76-9] and swertiamarin (II) [17388-39-5] in 0.1N NaHCO<sub>3</sub> was examined and it was found that they were readily decomposed and only 12% of I and 14% of II remained after 7 days. Therefore, preps. containing Gentiana Radix or Swertiae Herba dispensed with NaHCO<sub>3</sub> should be stored avoiding moisture.

L4 ANSWER 43 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1976:586652 HCAPLUS  
 DOCUMENT NUMBER: 85:186652  
 TITLE: Chemical constituents of Gentianaceae. XIX.  
 CNS-depressant effects of swertiamarin  
 AUTHOR(S): Bhattacharya, S. K.; Reddy, P. K. S. P.; Ghosal, S.;  
 Singh, A. K.; Sharma, P. V.  
 CORPORATE SOURCE: Dep. Pharmacol., Banaras Hindu Univ., Banaras, India  
 SOURCE: Journal of Pharmaceutical Sciences (1976), 65(10),  
 1547-9  
 CODEN: JPMSAE; ISSN: 0022-3549  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



I

AB CNS (central nervous system) activity of swertiamarin (I) [17388-39-5], a secoiridoid glucoside from *Swertia chirata*, was evaluated. An apparent anomaly, associated with the unanticipated finding that the alc. exts. (excluding mangiferin [4773-96-0]) of *S. chirata* significantly reversed the mangiferin-induced CNS-stimulating effects in albino mice and rats, was resolved. The results indicate that I and mangiferin antagonize each other in vivo and thereby reverse their CNS effects.

L4 ANSWER 44 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1976:437295 HCAPLUS

DOCUMENT NUMBER: 85:37295

TITLE: Studies on crude drugs originating from gentianaceous plants. II. Determination of swertiamarin, the major bitter principle of *Swertiae Herba* and related crude drugs

AUTHOR(S): Hayashi, Teruaki; Tsuji, Yoshitaka; Matuda, Taro

CORPORATE SOURCE: Res. Lab., Koshiro Chuji-Shoten Co., Ltd., Osaka, Japan

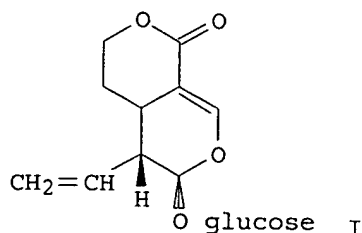
SOURCE: Yakugaku Zasshi (1976), 96(4), 498-502

CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

GI



AB Two new methods were developed for the determination of swertiamarin (I) [17388-39-5], the main bitter principle of the herb of *Swertia japonica* and of *S. pseudochinensis*. In the preparative thin-layer chromatog.-TLC uv method, I in the MeOH extractive of *Swertia* herb is separated by preparative TLC developing with 6:1:3 AcOEt-Pr(OH-H<sub>2</sub>O) (detected as a pink

spot by a PAN-uv Lamp) and is determined by the uv absorbance at 238 nm. In the TLC-densitometer method, the MeOH extractive containing I is developed on a TLC plate (Kieselgel 60F254) using the same solvent system, and the amount of I ( $R_f$  appr. 0.3) is determined by TLC densitometry, using a dual-wavelength TLC scanner. By these methods, the contents of I were 1-2.5% in Swertia Herba and 0.9-1.5% in Swertia Pseudochinensis Herba (both Osaka market products). It has also been found that the content of I in Swertiae Herba varies depending on the parts of the original plant and decreases in the order of flowers, leaves, stems and roots.

L4 ANSWER 45 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1973:496974 HCAPLUS  
 DOCUMENT NUMBER: 79:96974  
 TITLE: Stabilization of swertiamarin in water  
 INVENTOR(S): Ishida, Tatsuya; Ohsuka, Yasuhiko; Suzuki, Shigenobu; Mitome, Isao  
 PATENT ASSIGNEE(S): Pola Chemical Industry Co., Ltd.  
 SOURCE: Jpn. Tokkyo Koho, 3 pp.  
 CODEN: JAXXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 48019930	B4	19730618	JP 1970-123514	19701231
PRIORITY APPLN. INFO.:			JP 1970-123514	19701231

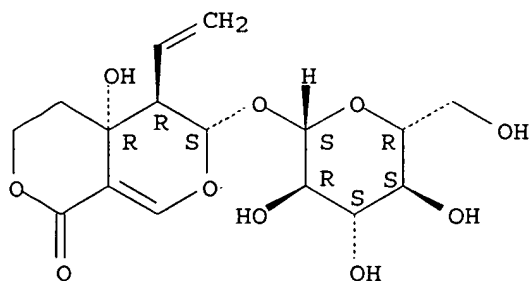
AB A solution of the title compound (I), the bitter principle of Gentianaceae, useful as drug and dermatol. cosmetics, was stabilized by addition of alc. (>30vol.%) and by pH adjustment to 4-9. E.g., 0.1% solution of I, pH 6, containing 70% EtOH, was quite stable on 6-month storage.

IT 17388-39-5  
 RL: BIOL (Biological study)  
 (pharmaceutical solution, ethanol stabilization of)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 46 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1968:16139 HCAPLUS  
 DOCUMENT NUMBER: 68:16139  
 TITLE: Isolation of swertiamarin  
 INVENTOR(S): Araki, Yasuo  
 SOURCE: Jpn. Tokkyo Koho, 4 pp.



CODEN: JAXXAD  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 42010926	B4	19670616	JP	19651213

AB C treatment of a swertiamarin (I)-containing extract in aqueous EtOAc, CHCl<sub>3</sub>-EtOH, Me<sub>2</sub>CO, or Me<sub>2</sub>CO-EtOAc removes impurities with little loss of I. Thus, 60 kg. Swerita japonica was extracted 3 times with 500 l. MeOH at 60° for 1 hr., the extract evaporated in vacuo to 120 l., treated with 240 l. H<sub>2</sub>O, and clarified to give 350 l. aqueous MeOH extract Spray drying gave 8 kg. powder. The powder (1.5 kg.) was extracted 3 times 35.1 H<sub>2</sub>O saturated EtOAc at room temperature The combined exts. were treated with C at 20-5°, evaporated to 5 l. at 30-5° in vacuo, and clarified to remove resin. Further concentration to 200-50 cc. and treatment with 500 cc. Et<sub>2</sub>O gave 10 g. colorless precipitate, useful as a medicine. Pure I, m. 112-14°, λ<sub>maximum</sub> 237 mμ, is a white, bitter powder.

L4 ANSWER 47 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1964:492629 HCAPLUS  
 DOCUMENT NUMBER: 61:92629  
 ORIGINAL REFERENCE NO.: 61:16143f-g  
 TITLE: New drug  
 PATENT ASSIGNEE(S): Yoshihide Hagiwara  
 SOURCE: 2 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Unavailable  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 39007783		19640518	JP	19620221

AB The Japanese drug Toyaku (50 g.) and 2 g. CaCO<sub>3</sub> were added to 750 ml. boiled EtOH, the mixture was refluxed 30 min. and filtered, and the residue extracted several times with 250 ml. EtOH at 40-5° and filtered to give 1.5 l. filtrate. The filtrate was evaporated in vacuo, 100 ml. water added, and the mixture kept overnight and filtered. To the filtrate was added 90 ml. 2% Pb(OAc)<sub>4</sub> solution, the mixture filtered to avoid precipitation of protein and excess Pb(OAc)<sub>4</sub>, and the filtrate concentrated in vacuo. The concentrated extract (8 g.) was dissolved in 30 ml. EtOAc and 3 ml. EtOH, refluxed on a water bath 30 min., and concentrated in vacuo to give 2-3 g. glucoside containing swertiamarin and gentianin; 2:1-2:0.02 in weight proportion.

L4 ANSWER 48 OF 48 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1935:24006 HCAPLUS  
 DOCUMENT NUMBER: 29:24006  
 ORIGINAL REFERENCE NO.: 29:3115c-d  
 TITLE: Constituents of lesser centaury (Erythraea centaurium)  
 AUTHOR(S): Kariyone, T.; Kashiwagi, K.  
 SOURCE: Yakugaku Zasshi (1934), 54, 1077-90  
 CODEN: YKKZAJ; ISSN: 0031-6903  
 DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Hacuerissey and Bourdier (C. A. 3, 427) have previously isolated a bitter crystalline glucoside "erythraurin" (I) from lesser centaury, but they gave no m. p. or anal. data. The erythrocentaurin, C<sub>27</sub>H<sub>24</sub>O<sub>8</sub>, of Macuehu (J. pharm. [4], 3, 265(1866)) is a tasteless crystalline substance. Kariyone and Matsushima (J. Pharm. Society Japan Number 540, 133(1927) and C. A. 24, 125) have isolated swertiamarin from the Japanese bitter herb Swertia japonica, which on hydrolysis gave one mol. each of erythrocentaurin (II), C<sub>10</sub>H<sub>8</sub>O<sub>3</sub> and glucose. On the assumption that II is an aglucone of I, I was hydrolyzed by emulsin and II was actually isolated from the hydrolytic product.

=&gt; =&gt; d stat que l11

```

L1      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  SWERTIAMARIN/CN
L3      213 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 OR ?SWERTIAMARIN?
L4      48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 (L) (?MEDIC? OR ?THERAP? OR
        ?PHARM? OR ?DRUG?)
L5      1 SEA FILE=REGISTRY ABB=ON  PLU=ON  CYTOCHROME P450/BI
L7      SEL  PLU=ON  L5 1- CHEM :      3 TERMS
L8      1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L9      51451 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L8 OR CYTOCHROME(2A) 450 OR
        CYP3A
L10     4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L9
L11     1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 NOT L4

```

=&gt; d ibib abs hitstr l11 1

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2003:696526 HCAPLUS  
 DOCUMENT NUMBER: 139:207740  
 TITLE: Dermal cytochrome P450 1A inhibitors and enhancers  
 INVENTOR(S): Yoa-Pu, Hu Oliver; Hsiong, Cheng-Huei; Wang, Chao-Jih;  
 Pao, Li-Heng  
 PATENT ASSIGNEE(S): Taiwan  
 SOURCE: U.S. Pat. Appl. Publ., 12 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003166583	A1	20030904	US 2002-79416	20020222
PRIORITY APPLN. INFO.:			US 2002-79416	20020222

AB The present invention provides dermal cytochrome P 450 1A (CYP1A) inhibitors, which include free base or pharmacol. acceptable salt of (-)- and (+)-epicatechin, (+)-limonene, 3-phenylpropyl acetate,  $\alpha$ - and  $\beta$ -naphthoflavone, apigenin, baicalein, baicalin,  $\beta$ -myrcene, catechin, etc. The CYP1A inhibitors can be co-administered with compds. with first-pass effect such as dermatol. drugs to improve the bioavailability of the drugs. The present invention also provides dermal CYP 1 A enhancers, which include (+)-catechin, (-)- and (+)-epicatechin, (+)-limonene, 3-phenylpropyl acetate, apigenin, baicalein, baicalin, etc. Examples were given showing the inhibitory effects on liver CYP1a activity of the compds.

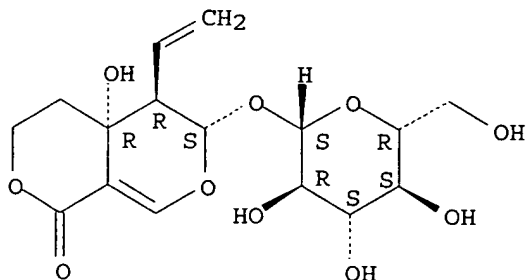
IT 17388-39-5, Swertiamarin  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
(dermal cytochrome P 450 1A inhibitors and  
enhancers)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-(β-D-glucopyranosyloxy)-  
4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> => d stat que l19

L1 1 SEA FILE=REGISTRY ABB=ON PLU=ON SWERTIAMARIN/CN  
L2 10 SEA FILE=REGISTRY ABB=ON PLU=ON (SWERTIAMACR/BI OR SWERTIAMAC  
ROSIDE/BI OR SWERTIAMAR/BI OR SWERTIAMARIN/BI OR SWERTIAMARINE/  
BI OR SWERTIAMAROSIDE/BI) NOT L1  
L3 213 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 OR ?SWERTIAMARIN?  
L4 48 SEA FILE=HCAPLUS ABB=ON PLU=ON L3 (L) (?MEDIC? OR ?THERAP? OR  
?PHARM? OR ?DRUG?)  
L5 1 SEA FILE=REGISTRY ABB=ON PLU=ON CYTOCHROME P450/BI  
L7 SEL PLU=ON L5 1- CHEM : 3 TERMS  
L8 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L7  
L9 51451 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR CYTOCHROME (2A) 450 OR  
CYP3A  
L10 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L9  
L11 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 NOT L4  
L12 SEL PLU=ON L2 1- CHEM : 20 TERMS  
L13 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L12  
L14 202 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 OR ?SWERTIAM?  
L18 14 SEA FILE=HCAPLUS ABB=ON PLU=ON (L3 OR L14) (L) INHIBIT?  
L19 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L18 NOT (L4 OR L11)

=> d ibib abs hitstr l19 1-5

L19 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1993:81674 HCAPLUS  
DOCUMENT NUMBER: 118:81674  
TITLE: Inhibition of scale adhesion in the polymerization of  
ethylenic monomers  
INVENTOR(S): Watanabe, Mikio; Ueno, Susumu; Usu, Masahiro; Yono,  
Masayoshi  
PATENT ASSIGNEE(S): Shin-Etsu Chemical Industry Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04266902	A2	19920922	JP 1991-28939	19910222
PRIORITY APPLN. INFO.:			JP 1991-28939	19910222

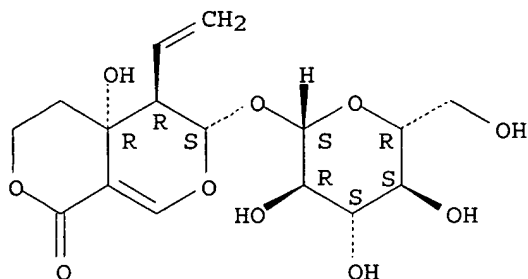
AB Scale adhesion is prevented in the polymerization of  $\text{CH}_2\text{:CR}_1\text{R}_2$  [ $\text{R}_1 = \text{H, Me; R}_2 = \text{H, CnH}_{2n+1}, \text{CO}_2\text{M (M = alkali metal, NH}_4^+), \text{CO}_2\text{CnH}_{2n+1}, \text{CN, Ph, C}_6\text{H}_4\text{R}_3 (\text{R}_3 = \text{H, OH, Me, CH:CH}_2), \text{OCOCnH}_{2n+1}, \text{OCnH}_{2n+1}, \text{CH:CH}_2]$  by using polymerizers, in which the monomer-contacting parts are covered with films containing xanthone-type natural colorants and PVA [saponification degree (A)  $\geq 70$  mol%]. A solution containing isogentisin and Poval C-25 (PVA; A  $\geq 99.0$  mol%) was used for coating on stainless steel polymerizer in emulsion polymerization for ABS preparation

IT 17388-39-5, Swertiamarin  
 RL: USES (Uses)  
 (scale inhibitors containing PVA and, for polymerizing ethylenic monomers)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:587302 HCAPLUS

DOCUMENT NUMBER: 109:187302

TITLE: Chemistry and pharmacology of *Gentiana lactea*

AUTHOR(S): Schaufelberger, Daniel; Hostettmann, Kurt

CORPORATE SOURCE: Ec. Pharm., Univ. Lausanne, Lausanne, CH-1005, Switz.

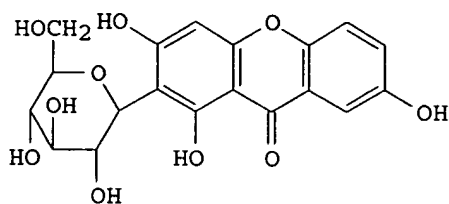
SOURCE: Planta Medica (1988), 54(3), 219-21

CODEN: PLMEAA; ISSN: 0032-0943

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

AB Flavonoids, secoiridoids, and xanthenes of *G. lactea* (Gentianaceae) were investigated and 14 compds. were identified, among these the previously undescribed neolancerin (I). The known constituents of *G. lactea* include bellidifolin, bellidifolin-8-O-glucoside, deacetylcentapicrin, demethylbellidifolin, demethylbellidifolin-8-O-glucose, gentiopicrin, isoorientin, isovitexin, loganic acid, mangiferin, swerchirin, sweroside, and swertiamarin. Xanthenes with 1,3,5,8-substitution patterns were tested for inhibition of monoamino oxidase (MAO). Bellidifolin is a strong and selective inhibitor of MAO A in vitro.

L19 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1985:605810 HCAPLUS

DOCUMENT NUMBER: 103:205810

TITLE: Effects of iridoid compounds on RNA and protein biosyntheses in Sarcoma 180 cells

AUTHOR(S): Huh, S. O.; Kim, J. H.; Chang, I. M.

CORPORATE SOURCE: Dep. Chem., Dongguk Univ., Seoul, 110, S. Korea

SOURCE: Saengyak Hakhoechi (1985), 16(2), 99-104

CODEN: SYHJAM; ISSN: 0253-3073

DOCUMENT TYPE: Journal

LANGUAGE: Korean

AB To investigate a possible biol. activity (antitumor) of iridoid glucosides, 6 compds., aucubin [479-98-1], catalpol [2415-24-9], gardenoside [24512-62-7], geniposide [24512-63-8], rehmannioside D [81720-08-3] and swertiamarin [17388-39-5], were studied in relation to their potential effects on RNA and protein biosyntheses in murine tumor cell, sarcoma 180, in vitro. Protein biosynthesis was slightly inhibited by aucubin, gardenoside and swertiamarin. The degree of inhibition of RNA biosynthesis by those iridoids appeared to be more sensitive than was that of protein biosynthesis. When aucubin was pretreated with  $\beta$ -glucosidase to produce its genin form and the sarcoma 180 cells were exposed to this aucubigenin [64274-28-8], protein and RNA biosyntheses in the cells were markedly inhibited. Apparently, the biol. active form of these iridoid compds. is the hydrolytic product of the glycoside, i.e., the genin form. Further, sarcoma 180 cells used in these expts. appear to lack  $\beta$ -glucosidase, since the inhibitory effects of the iridoid glucosides were so slight, i.e., the glucosides were not hydrolyzed by the enzyme to their genin forms.

IT 17388-39-5

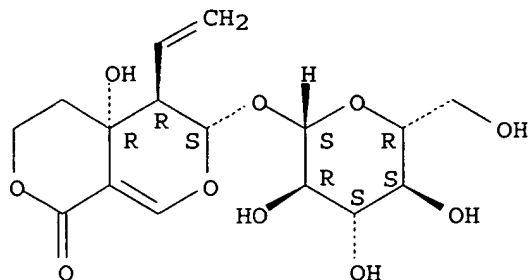
RL: BIOL (Biological study)

(protein and RNA formation response to, neoplasm inhibition in relation to)

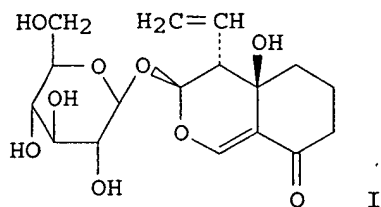
RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-( $\beta$ -D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L19 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1983:137499 HCAPLUS  
 DOCUMENT NUMBER: 98:137499  
 TITLE: Antispastic effect of swertiamarin  
 AUTHOR(S): Lei, Weiya; Shi, Quantao; Yu, Sichang  
 CORPORATE SOURCE: Yunan Inst. Pharmacol., Peop. Rep. China  
 SOURCE: Zhongcaoyao (1982), 13(10), 464-6  
 CODEN: CTYAD8; ISSN: 0253-2670  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese  
 GI

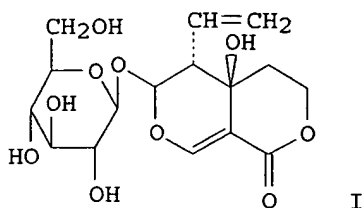


AB The contraction of isolated duodenal and uterine smooth muscle of rats and rabbits was markedly inhibited swertiamarin (I) [17388-39-5]. Acetylcholine-, BaCl<sub>2</sub>-, or histamine-induced ileal spasm in guinea pig was antagonized by I. I also antagonized pituitrin- and acetylcholine-induced excitation of rabbit small intestine and uterus. At dosage of 60-100 mg/kg, I showed effective antispastic effect. No death was observed in mice that received 10.0 g I/kg (stomach infusion), 8.0 g I/kg (i.p.), and 5.0 g I/kg (i.v.), indicating that the toxicity of I is very low. Thus, I is a safe and effective antispastic agent.

L19 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1979:409485 HCAPLUS  
 DOCUMENT NUMBER: 91:9485  
 TITLE: Antiinflammatory secoirridoids  
 INVENTOR(S): Hayashi, Teruaki; Kubo, Michinori  
 PATENT ASSIGNEE(S): Koshiro, C., and Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 54026323	A2	19790227	JP 1977-89951	19770726
JP 60041641	B4	19850918		
PRIORITY APPLN. INFO.: GI			JP 1977-89951	A 19770726



AB Secoirridoids isolated from various medicinal plants (*Gentiana scabra*, *G. macrophylla*, *Swertia japonica*, etc.) are antiinflammatory agents. Thus, the root or stem of *G. scabra* was chopped, extracted with warm anhydrous EtOH, filtered, and evaporated at 50° under reduced pressure to give yellow substances. The residue was worked up and subjected to silica gel column chromatog., and active fractions were pooled and evaporated to give gentiopicroside (I) [20831-76-9], m. 181°. The effectiveness of I was tested in carrageenin-induced foot edema in rats.

IT 17388-39-5

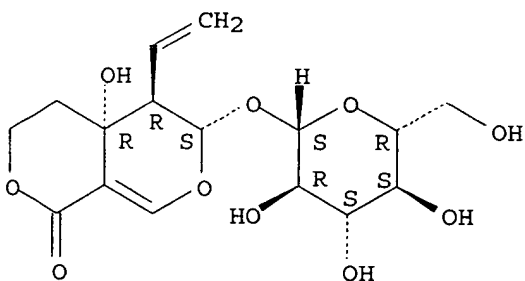
RL: BIOL (Biological study)

(of *Swertia japonica*, as inflammation inhibitor)

RN 17388-39-5 HCAPLUS

CN 1H,3H-Pyrano[3,4-c]pyran-1-one, 5-ethenyl-6-(β-D-glucopyranosyloxy)-4,4a,5,6-tetrahydro-4a-hydroxy-, (4aR,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=>